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# E. MERCK'S ANNUAL REPORT

:: OF RECENT ADVANCES IN ::  
PHARMACEUTICAL CHEMISTRY  
:: :: AND THERAPEUTICS :: ::

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Medical  
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1912 :: VOLUME XXVI

E. MERCK, CHEMICAL WORKS, DARMSTADT  
1913



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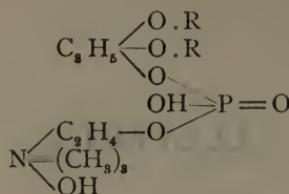
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## LECITHIN.

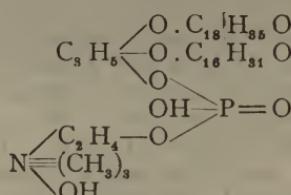
In the economy of living cells belonging to the vegetable and animal kingdoms, a very important part is played by a certain group of bodies, which are generally spoken of collectively as "lipoids"\*\*). Among the best known members of this group are the cholesterins and lecithins. While the cholesterins are organic combinations free from nitrogen and phosphorus, the lecithins contain both nitrogen and phosphorus. They are grouped together as a special class of bodies, the so-called "phosphatides"\*\*\*), comprising a large number of representatives. The phosphatides are characterised by containing one or more molecules of phosphoric acid, an alcohol (for example glycerin), one or more fatty acid radicles (for example stearic or oleic acid) and one or more nitrogenous bodies (such as choline and allied substances). Lecithin, or rather the lecithins, are phosphatides of this description. The theoretical formula of the lecithins is as follows:

\*) The word "lipoid" is derived from the Greek  $\lambda\acute{e}πος$  = fat. It denotes fatty substances which contain phosphorus, or phosphorus and nitrogen, or neither of these elements, and which have special functions to perform in the cell. An exact definition of the term "lipoid" cannot be given. Kletzinsky understood it to mean those substances which cannot be saponified and which may be extracted from animal cells by means of alcohol and ether. If their non-saponification be left out of account, for it applies to cholesterin but not to lecithin, the designation "lipoid" may still be defined in the terms of the author mentioned above, for Overton considers it to denote all those components of the cell which, like fat, will dissolve in ether, chloroform and similar organic liquids. Kraus termed lipoids "noble fats" to distinguish them from fats.

\*\*) Lecithin is a mono-amino-mono-phosphatide, which denotes that still more complex substances exist, e. g., di-amino-mono-phosphatides, mono-amino-di-phosphatides, di-amino-di-phosphatides, tri-amino-mono-phosphatides, etc. These bodies have not as yet been exhaustively investigated. (Compare Thudichum.) It should be noted that at the end of this article a detailed list of the literature is given, arranged according to authors. In the text the authors are mentioned without foot-notes.



It is highly probable that other substances containing nitrogen and allied to choline may occur in natural lecithin, but so far choline alone has been demonstrated with certainty in the decomposition products of the lecithins. The radicles of stearic, palmitic and oleic acid (R in the above formula) are present in the form of esters with the glycerin radicle in the lecithin molecule. It has not yet been possible to determine whether one molecule always contains either two similar or two different acid radicles. Although in the examination of lecithin obtained from egg yolks stearic acid and palmitic acid or oleic acid are usually found, this is not a proof that these acids are derived from a single molecule; for a mixture of stearyl and palmityl-lecithin, or of stearyl and oleic acid-lecithin may equally well be present. But in the textbooks of physiology or of physiological chemistry, lecithin from egg yolks is occasionally represented by the assumptive formula of stearyl-palmityl-lecithin:



The structure of this formula may most probably be traced back to the statements of Thudichum; in his opinion a lecithin molecule always contains one saturated and one unsaturated fatty acid residue. According to him, every true lecithin contains at least one fatty acid radicle and always represents a mono-amino-mono-phosphatide, e. g., the molecule contains only one atom of nitrogen and one atom of phosphorus.

It is generally assumed that the lecithin from egg yolks is mainly stearyl-lecithin and the lecithin obtained from plants mainly oleic acid-lecithin. In how far this assumption is supported by facts cannot be decided on the strength of the researches on the lecithins so far carried out. It is indeed

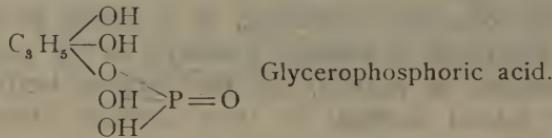
doubtful whether the above formula definitely explains the constitution of the natural lecithins\*). The investigations of MacLean, Otolski, Cousin, Erlandsen, Henriques and Hansen have shown that the lecithins, besides containing choline, also possibly contain other nitrogenous disintegration products (pyridine) and other unsaturated fatty acids (linoleic acid and linolenic acid). This may also be inferred from the relatively high iodine number of the lecithins, which is not sufficiently explained by their content of oleic acid. Nor can it be decided whether calcium and iron, which always accompany the lecithins, form an essential part of the lecithin molecule or are merely impurities; thus no great weight can be attached to the constitutional formula of lecithin. Further, Malengreau and Prigent, as a result of hydrolytic experiments, have expressed doubt as to the possibility of an ester-like combination between choline and phosphoric acid. It is certainly true that the natural lecithins, however carefully they are purified, always represent mixtures of various lecithins. The physical condition of pure commercial lecithin, which is waxy and occasionally somewhat crystalline, is in favour of this view; and it is justifiable to assume, according to the present position of research on lecithin, that the separate lecithins which constitute natural lecithin, in their absolute chemical individuality and purity, are crystalline bodies.

The solution of this problem is, however, of more chemical than physiological or therapeutic interest. As is evident from an investigation by Stepp, those lecithins alone are of physiological or therapeutic importance which are produced by the living organism itself for its own use. It is therefore probably justifiable in therapeutics to speak of pure lecithin when this consists solely of lecithins without admixture of albumins or of lecithalalbumins. My Lecithinum ex ovo purissimum is a preparation of this nature.

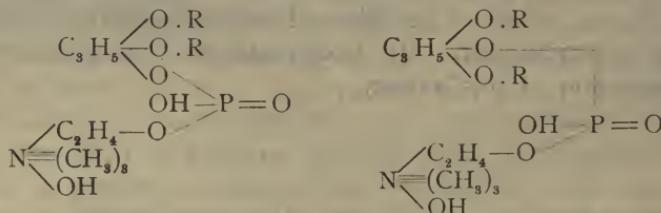
\* According to Thierfelder and Stern, other phosphatides besides lecithin occur in egg yolks. These have also been found by Thudichum, Hammarsten, Erlandsen and others in various animal organs.

The discovery of lecithin is usually attributed to Gobley (1846), although long before him Vauquelin (1811) and Couerbe (1834) found and described phosphorus-containing fats in the brain, which were probably identical with lecithin. Fremy, a pupil of Couerbe, named Vauquelin's substance "oleophosphoric acid", as he found its products of decomposition to consist of glycerin, phosphoric acid and oleic acid. In conjunction with Valencienne he isolated the same substance from the roe of fish. But Gobley was the first to prepare it from the yolk of eggs, and he called it "matière visqueuse", and later, on account of its origin, "lecithin", from *λεκυθος* (= yolk of egg)\*). He was also the first to recognise the principal component of lecithin possessing physiological importance, namely glycerophosphoric acid, which is obtained by the careful saponification of lecithin; he thus established the basis for the constitution of the lecithin molecule which is still fairly generally accepted. The basic component of lecithin, choline, was discovered by Liebreich and Strecker.

Lecithin is therefore regarded as a glycerophosphoric acid



in which the hydrogen atoms of the hydroxyls of glycerin are replaced by fatty acid radicles, and one hydrogen of the phosphoric acid residue by a choline radicle. Theoretical consideration shows that two possible formulas exist, one symmetrical and one asymmetrical, according to the position of the fatty acid residues in the glycerin, thus:



\*) Strecker's view (*Annalen der Chemie und Pharmazie* 1868, Vol. 72, p. 77) that the word lecithin is derived from *ληκυθος* (= oil jar) and should therefore be written lecythin, is erroneous.

Since lecithin is optically active and as, according to Willstätter and Lüdecke and also according to Power and Tu tin, the glycerophosphoric acid derived from lecithin possesses rotatory power, Ulpiani expressed himself in favour of the asymmetrical formula. Speculations of this kind are, of course, only of theoretical interest. Possibly the synthesis of the lecithins, which has not as yet been successfully carried out, will throw light on the question of the constitution of lecithin. Hundeshagen, as the result of an unsuccessful synthesis of lecithin, claimed to have proved the truth of Strecker's statement that lecithin was not a salt of di-stearyl-glycerophosphoric acid and choline, but an ester-like combination of the two substances, in which the basic character of choline was retained. The choline salt of di-stearyl-glycerophosphoric acid obtained by Hundeshagen had quite different properties than lecithin. Kade's attempts to prepare lecithin synthetically must also be regarded as failures from a practical point of view.

#### Occurrence of Lecithin.

Lecithin is so widely distributed in the human and animal organisms that it has been concluded, though not without contradiction, that no organ exists which does not contain lecithin. Thus the phosphatide is found, according to Hermann, Hoppe-Seyler, Manasse, Abderhalden and Peritz in the blood; according to Miescher in pus; according to Gobley, Liebreich, Thudichum and Koch in the brain; according to Dunham, Rubow, Krehl, Nerking, Hefftner, Baskoff, Noel Paton, MacLean, Bischoff and others in the heart (cardiac muscle), kidneys, suprarenal glands, liver, lungs and spinal cord, and according to Fränkel in the pancreas, muscles, testicles and submaxillary gland as well; according to Chevalier and Koch in nerve tissue (sciatic); according to Glikin, Rolle and Otolski in bone marrow; according to Thudichum, Long and Gephart in bile; according to Dezani, Vacheron and Miescher in the sperm; according to Donath in the cerebro-spinal fluid; according to Wallis and Schölberg in ascitic fluid, etc. Further, according to Hoppe-Seyler, it is a component of caviare; according to Burow, Tolmatscheff, Koch,

Vageler, Siegfeld, Glikin, Dornic and Daire and Marre it is a component of milk and consequently of butter, as has been proved by Krampelmeyer, Jaekl and Bordas. The percentage of lecithin indicated by the various authors in human or animal organs is as follows:

Blood 0·2 p. c.	Human fat 0·05 p. c.
Blood corpuscles 0·46 p. c. (1·8 p. c.)	Muscles 0·8 p. c.
Brain 16 p. c.	Testicles 1 p. c.
Heart 4·5 p. c.	Submaxillary gland 1 p. c.
Cardiac muscle 12·5 p. c.	Nerve tissue 17 p. c. (of the dry tissue)
Kidneys 8·5 p. c.	Sciatic nerve 33 p. c. (of the dry tissue)
Suprarenal gland 2·5 p. c.	Sperm 1·5 p. c.
Liver 4·3 p. c.	Milk 0·06 p. c.
Bile 0·15 p. c.	Butter 0·17 p. c.
Lung 1·5 p. c.	Yolk of egg 12 p. c.
Spinal cord 11 p. c.	Rabbit (living) 0·5 p. c.
Marrow 3 p. c.	Hedgehog (living) 0·8 p. c.
Pancreas 0·5 p. c.	
Thymus 7·5 p. c.	

In the vegetable kingdom lecithin is also very frequently found. It was first discovered in plants by Knop in 1860, but its general distribution throughout the vegetable kingdom was first established by Töpler. It is always abundantly present in seeds, buds and young shoots, a fact which indicates its great importance in the growth of young plants. The lecithin content of various seeds is specially reported upon by Schulze, Forti, Maxwell, Bernardini and Chiarulli; lecithin in vegetable oils by Schlagdenhauffen and Reeb, Stellwaag, Jacobson, Riegel and others; in sugar cane by Shorey; in yeast by Hoppe-Seyler, Himberg and Sedlmayr; in leaves, blossoms, fruits, etc., by Vageler; in fungi by Heinisch, Zellner and Lietz; in grape pips and wine by Rosenstiehl, Funaro and Barboni, Muraro, Bicciardelli and Nardinocchi, Salvadori and Mazzaron; and the occurrence of lecithin in the vegetable kingdom generally by Kraetzschmar, Heckel and Schlagdenhauffen, Stoklasa, Hanai, Marchlewski, Winterstein and Hiestand and others.

The content of various seeds, vegetable oils, etc., is given as follows in the literature:

Barley 0·7 p. c.	Cantharellus cibarius 1·3 p. c.
Wheat 0·6 p. c.	Lettuce 0·36 p. c.
Rye 0·6 p. c.	Rhubarb 0·33 p. c.
Peas 1·2 p. c.	French beans 0·25 p. c.
Lentils 1 p. c.	Green peas 0·15 p. c.
Beans 0·8 p. c.	Green tomatoes 0·25 p. c.
Linseed 0·9 p. c.	Yeast (dry) 2 p. c.
Vetch seeds 1·2 p. c.	Wine 0·03 p. c.
Lupin seeds 2 p. c.	Fat of melon seeds 0·6 p. c.
Pumpkin seeds 0·4 p. c.	„ „ lupin seeds 7·5—50 p. c.
Poppy seeds 0·25 p. c.	„ „ peas 30—50 p. c.
Maize 0·25 p. c.	„ „ vetch seeds 13—21 p. c.
Soya-bean oil 0·15 p. c.	„ „ rye 8 p. c.
Ergot 1·7 p. c.	„ „ wheat 7 p. c.
Toadstools 1·4 p. c.	„ „ barley 7 p. c.
Yellow boletus 0·6 p. c.	„ „ oats 11·5 p. c.
Mushrooms 0·9 p. c.	„ „ fenugreek seeds 1·5 p. c.
Morel 1·6 p. c.	„ „ maize 1·5 p. c.

However, lecithin does not only occur as such, but especially in plants in combination with other substances. Thus ovo-vitellin, described by Hoppe-Seyler, is a combination of lecithin with albumin; jecorin described by Drechsel, Boskoff, Erlandsen and others, is a combination of lecithin with glucose or galactose and other substances; and protagon, which occurs in the central nervous system and in the brain and has been investigated and described by Liebreich, Hoppe-Seyler, Diakonow, Strecker, Gamgee, Blankenhorn, Baumstark, Ruppel, Kossel and Freytag, is a combination of lecithin with cerebrosides\*). Protagon is described by Kossel, Ruppel and others as a crystalline substance, soluble in hot alcohol and which swells up in water.

### Physiology of Lecithin.

Special attention has been paid to the study of the origin and significance of lecithin in the vegetable world by Maxwell, Stoklasa, Staniski, Marchlewski, Hanai and Koch. Even though the results of their investigations

\*) Cerebrosides are bodies containing nitrogen but no phosphorus, which on hydrolysis produce sugar.

have not rendered the chemistry of lecithin formation as clear as might be desired, yet they have shown that lecithin may and usually does occur in all parts of plants. From this fact alone it may be concluded that it is a very important or indispensable body in the plant.

Maxwell attempted to prove that the phosphorus present in seeds in an inorganic form was changed during germination to the organic form, during which process lecithin was produced. The intermediate stages passed through by the phosphoric acid are unknown. In the transition from the vegetable to the animal kingdom the organic combination is, in the author's opinion, retained. The lecithin of a hen's egg, on the other hand, changes when the egg is hatched into inorganic phosphorus compounds, and as a mineral phosphate plays a part in the bone-formation of the developing animal. But in the later stages of hatching, as Maxwell showed, the opposite process may occur. The most interesting fact brought out by Maxwell's researches is that the animal organism is capable of changing inorganic phosphorus into organic compounds. As in the opinion of some observers, to which reference will be made later, the lecithin ingested with the vegetable food is decomposed in the animal intestine and absorbed as phosphoric acid (glycerophosphoric acid), lecithin synthesis must occur in the animal and human organism, for it would otherwise be impossible to explain the origin of the richness in lecithin of the animal organism. Reicher has recently also favoured this opinion.

Stoklasa, from his own observations, formed the opinion that by far the greater part of the phosphoric acid of plants was present in the form of organic compounds. Besides the nuclein compounds, lecithin is an important example of this class. It probably plays an important part in the processes of assimilation and dissimilation. In testing the lecithin content of seedlings, leaves and blossoms, the author found that the lecithin was not decomposed by germination, but that no lecithin was formed except when, under the influence of light and chlorophyll, carbonic acid assimilation had set in. He even showed that in the absence of chlorophyll (in the leaves) no lecithin is formed and that in etiolated seedlings the lecithin is used up or decomposed. It is possible that during the first vegetative period lecithin, under the influence of light, assists in the formation of chlorophyll in the seedling.

The greatest amount of lecithin is probably formed in fresh green leaves at the time when the function of assimilation is at its height, an assumption made probable by the fact that the amount of lecithin in leaf-buds is only half as great as that in fully developed leaves, and that it rapidly disappears as the leaves grow older; the chlorophyll is reduced and xanthophyll makes its appearance.. According to this, there is a close connection between the formation of chlorophyll and lecithin. Stoklasa even considers that lecithin may be a product of assimilation in the chlorophyll corpuscle itself. In agreement with this conjecture is the observation that certain plants, if placed in the dark at the time of their most active growth, soon show a considerable diminution of lecithin in their leaves, as compared with those which are allowed to develop in the light. It has not yet been discovered in what way lecithin assists in chlorophyll formation, but according to Stoklasa, it is certain that no chlorophyll can be produced in the absence of light and phosphorus. Thus even if lecithin is not a part of the chlorophyll corpuscle itself, as was formerly assumed by Marchlewski, yet it appears to participate in chlorophyll formation and to supply the necessary phosphorus. From the leaves lecithin travels by way of the stems into the blossoms, where it may perhaps assist in fertilisation, and thence by the fruits into the seeds. It is by no means certain, however, that the green leaves are the sole producers of lecithin; it is quite probable that plants and animals are able to build up lecithin in certain organs and from certain substances, as is the case for example in yeast and in fungi.

Stoklasa's observation that phosphorus is present in plants chiefly in organic form is confirmed by the results of Staniski's researches. This observer found only very small amounts of inorganic phosphoric acid in the seeds of millet in comparison with the amount of organic phosphorus present. He found that in millet lecithin formation was at its height during the period of seed development, and that the maximum amount of lecithin was contained in the plant during the period of panicle formation. Thus it is justifiable to draw the conclusion that lecithin has important functions to perform in connection with flower and seed formation.

Hoppe-Seyler pointed out the close relationship between lecithin and chlorophyll mentioned above. He even placed chlorophyll in the group of lecithins. Although this

view has not as yet been confirmed, it is supported to some extent by Stoklasa's researches. Furthermore, Marchlewski, Bode and Kohl have put forward theoretical considerations according to which chlorophyll represents a lecithin in which the fatty acid radicles\*) are replaced by special, coloured complexes (chlorophyllanic acids), or these complexes themselves are chlorophyll combined with lecithin\*\*).

Hanai's statements supplement Stoklasa's communications. He made the observation that the old, green leaves of *Thea Chinensis* lose their lecithin in spring, and that the young, growing leaves are very rich in lecithin. He therefore places lecithin among the reserve substances, which are stored in certain parts of the plant (as, for example, in the bark of the plant just mentioned) until the next period of growth, when they are supplied to the new shoots\*\*\*).

The conclusions drawn by Vageler from his investigations are deserving of special mention. According to these, the lecithins are inseparably bound up with metabolism and with the vital processes of the plant generally. The content of phosphatides increases up to the time of development of the fruit, the zenith of development, and decreases as the fruit ripens. Lecithin has, in the author's opinion, probably nothing to do with fat, with which others often consider it to be in relation. Like Koch, he seeks the function of lecithin in the cell primarily as an oxygen carrier, but also in the colloidal character of the phosphatides, "for the substratum of life itself, protoplasm, which is still in many respects so enigmatical, is a colloid."

The physiological significance of the fatty acids contained in lecithin and of choline is explained by Koch. According

\*) Compare the formula for lecithin on page 2.

\*\*) According to W. Pfeffer, (*Pflanzenphysiologie* 1897, 2nd. edition, Vol. 1, p. 478) the lecithins are perhaps necessary for the construction of protoplasts. However, it is not yet known whether they take part in the conversion of fats. The occurrence of choline in plants probably depends upon the conversion of lecithins. According to Willstätter, chlorophyll contains no phosphorus, whereby the theories of the authors mentioned above are incorrect. Compare also Marchlewski, *Biochemische Zeitschrift* 1908, Vol. 10, p. 131.

\*\*\*) According to Jost (*Pflanzenphysiologie* 1908, p. 184), however, the lecithins are not reserve substances, but constructive materials for protoplasm, and for this reason they are not decomposed during germination of the seeds.

to him, the lecithins are of importance for the life of the cell in two ways. For in conjunction with the albumins in colloidal solution, they constitute the basis for the formation of the necessary viscosity, on account of the ease with which they are influenced by ions (Na, Ca.). Further, by means of their unsaturated fatty acids they take part in oxygen metabolism, and by their methyl groups, which are combined with nitrogen, in other reactions not yet known. Phosphoric acid, although in some respects the nucleus of the whole, does not, in Koch's opinion, play any part in metabolism; Halliburton has shown that the amount of phosphorus in degenerated nerves does not begin to decrease before the eighth day. The author explains the fact that the residues of the unsaturated fatty acids are capable of taking part in oxygen metabolism by the ease with which they are oxidised; this is also known to be the case with lecithin which has been in contact with the air for some time. But it has not yet been proved that the lecithins may be regarded as oxygen carriers. The physiological significance of the nitrogen group may, according to Halliburton, be recognised by the fact that in certain diseases of the nervous system, such as general paralysis, a considerable amount of choline passes into the cerebro-spinal fluid.

As in the vegetable kingdom, so in the animal kingdom, lecithin, as I mentioned above, is present in almost every organ. It is present in comparatively large amounts in the principal organs, and the conclusion may consequently be drawn that it also performs important functions in the economy of the animal cell. The nature of these functions cannot be stated with certainty. Nor has it been conclusively ascertained whether lecithin is formed in the animal organism, whether it is ingested with the food, or whether both these processes take place. The results of the investigations of various observers afford some elucidation of the matter.

Bokay found that lecithin was split up in the intestine by the fat-splitting ferment of the pancreas, or putrefactive ferment, into fatty acids, choline and glycerophosphoric acid. As he was unable to demonstrate the presence of phosphoric acid in ethereal and alcoholic extracts of the faeces, he concluded that lecithin or its decomposition products were absorbed and used up by the organism. In agreement with this conclusion is the fact investigated by him that the amount

of phosphoric acid in the urine is substantially increased after the ingestion of lecithin. Glycerophosphoric acid is absorbed from the intestine in the form of a salt, and is not, according to Hasebrök, further broken down into glycerin and phosphoric acid. Grosser and Husler, on the other hand, think it improbable that glycerophosphoric acid passes directly from the intestine into the organism, as they succeeded in isolating a ferment, the so-called glycerophosphotase, from the intestinal and renal cells which splits up glycerophosphoric acid without leaving a residue. They therefore assume that lecithin is completely broken down in the intestine and is built up again from its elements in the tissues. The fatty acids, like the fats taken in with the food, are partially absorbed in the form of salts of fatty acids and partially excreted. Choline is further broken down with formation of carbonic acid, ammonia and methane. As lecithin is said to be comparatively readily broken down, it is probably safe to assume that lecithin is not absorbed as such in the intestine; but this does not prove that it may not be partially absorbed unaltered and carried to the circulation. Miescher's observation on Rhine salmon is generally cited as a typical example of lecithin formation in the animal organism. According to this, a comparatively large amount of lecithin is formed in the sexual organs of these fishes during the hunger period, which is said to occur as they wander up stream. The necessary phosphorus is presumably supplied by certain muscles of the fish. Paton also attempted to prove that in salmon inorganic phosphorus changes into organic phosphorus, however the assertions of Paton and Miescher can only be accepted if it be proved that during their sojourn in fresh water these fishes really take in no nourishment. This was doubted by Pütter. Römann, from experiments on mice, concludes that the animal organism is capable of forming lecithin, for the mice increased and continued their development on lecithin-free food. But in similar experiments carried out by Stepp and Röhl the experimental animals perished. According to Röhl, mice fed exclusively on rice always perish in a few weeks, whereas on the addition of a small amount of lecithin their development continues normally. He therefore considers lecithin to be an essential component of food, which cannot be constructed from its elements in the mammalian body. On the other hand, according to Fingerling's observations,

ducks are apparently able to produce large amounts of lecithin from inorganic phosphorus. It must also be assumed that glycerophosphoric acid which has been absorbed is made use of in certain organs for the production of lecithin. The choline required for this purpose has been shown to be present in various parts of the organism (Kinoshita\*). Mulinon, Bernard and others point to the suprarenal glands as the seat of formation of lecithin. Moreover, lecithin appears to be capable of being split up by ferments in certain organs. Coriat, for example, believes an enzyme to be present in the brain, which decomposes lecithin with separation of choline. He did not succeed in isolating this enzyme, but he proved that its action was destroyed by heating.

After Bókay had demonstrated that lecithin could be split up by the secretion from the small intestine, P. Mayer attempted to establish which of the ferments of the small intestine (trypsin, erepsin, lipase) caused this disintegration. He found that lecithin was abundantly split up by steapsin and that under certain conditions the fatty acids separated in a crystalline form. According to this, the behaviour of lecithin is identical with that found by Connstein in the fermentative decomposition of the true fats. Mayer believes his observations to show that the enzymes do not react in the same way upon d- and l-lecithin.

Schumoff-Simanowski and Sieber also confirm the action of pancreatic and gastric steapsin in splitting up lecithin, whereas their tests with lipase of blood or blood serum gave a negative result. It is not capable of splitting off fatty acids from lecithin. It is indeed possible, with the help of this negative character, to distinguish lipase from other lipolytic enzymes. Lecithin is, on the other hand, decomposed by vegetable ferments, especially by the ferment of Ricinus communis, with separation of fatty acids.

But the results of the authors mentioned above do not appear to correspond entirely with all the facts, if they are

\*) Choline is said by Lohmann to occur in the suprarenal glands, by von Fürth and Schwarz in the thyroid gland and intestinal extracts, by Schwarz and Lederer in the thymus, spleen and lymphatic glands, by Kutscher in flesh, by Letsche in serum, by Jacobsen in bile, by Cramer in the brain, by Böhm in the placenta, by Gautrelet in the kidneys, ovaries, testicles and pancreas.

compared with the results obtained by Slowtzoff, Stassano and Billon. According to these authors, lecithin is not by any means readily decomposed and it is doubtful whether it is decomposed by the action of putrefactive bacteria and pancreatic ferment. Thus Stassano and Billon found that neither activated pancreatic juice nor gastric juice act upon lecithin; this was confirmed by Slowtzoff for fresh lecithin, but he observed the decomposition of older (oxidised) lecithin. He also confirmed the observation that choline was separated from lecithin which had been stored for some time, even when boiled, alkaline ferment solution was used. Independently of the separation of choline, saponification of lecithin by means of pancreatic juice, e. g., by steapsin, apparently occurs. As lecithin is readily emulsified in the presence of bile and albumoses, and as Stassano and Billon claimed to have observed that lecithin, when injected subcutaneously, was taken up by the leucocytes which had migrated to the site of injection, and that by feeding on lecithin the latter apparently passed into the lymph of the thoracic duct, Slowtzoff conducted experiments which showed that lecithin, when administered internally, is in part ingested unchanged, as could be recognised by the appearance of lecithin in the lymph. As regards the splitting up of lecithin in the intestine, it occurs, according to Slowtzoff, in the duodenum where it cannot, in his opinion, be caused by putrefactive bacteria.

The results of the investigations of the observers mentioned above lead to the assumption that the lecithin taken in with the food is partly absorbed as such and partly split up. Slowtzoff assumes that like the fats it can be gradually reconstructed in the organism by synthesis. The proof of this may be sought in the fact that the same or very similar results have been achieved in therapy with the salts of glycerophosphoric acid (compare Merck's Report 1911, pages 1 to 30) as with lecithin.

With regard to the action on lecithin and its decomposition by ferments (lipase, diastase) reference may also be made to the publications of Lapidus and Terroine.

The investigations carried out by Glikin are of much value for the biological significance of lecithin. He points out that birds and mammals show a greater or less content of lecithin in the bones or the whole body, according as to whether they are born naked and helpless, or independent and

with their senses developed. Thus the amount of lecithin in cats and dogs, which are born blind and helpless, is greater than that in guinea-pigs, which immediately after birth are able to feed on cabbage and turnips like the fully developed animals and are not dependent upon mother's milk; similarly insessorial birds contain more lecithin than autophagous birds, which is indeed clearly shown in the eggs of these birds. Man, also, who comes into the world helpless, shows a very high percentage of lecithin in the bone marrow, which is only appreciably diminished when growth proceeds more slowly, or ceases. He also established the fact that the bone marrow of young animals contains far more lecithin than does that of fully developed animals, and that this store of lecithin diminishes as the animal grows and that new-born animals come into the world with a large supply of lecithin. From these observations it is evident that lecithin represents a highly significant factor in the growth of animals, even though nothing is yet known of the finer biological processes involved in the utilisation of lecithin in the cell and in the organism.

But in order to form a conception of the functions of the lecithins or of the lipoids in general, the colloidal nature of these substances must primarily be taken into account; and also their capability of forming solutions and compounds, which are readily decomposed, with other substances of importance in the construction and the life of the cell. It must also be taken into consideration that certain concentrations of lipoids are more soluble in solutions of alkaline salts than in other salt solutions. It is assumed that by an increase in the concentration of the salt by the entrance of calcium salts into the cell with consequent separation in flakes of the lipoids, membranes are formed which are permeable, impermeable or semi-permeable to certain solutions. The so-called semi-permeable membranes, especially, appear to be of importance to the life of the cell, as they serve to keep within bounds the entrance and exit of substances.

In the interior of the cell, according to Meyer, it is through the intervention of the lipoids that the whole of the contents do not join to form a homogeneous mass, but that the thousand particles forming the cell, with all their different chemical affinities, remain side by side, drawn up in order and at a measured distance; on the surface, however, they constitute a guard against too rapid streaming in and out

of water, and against the penetration of all the salts dissolved in the blood and in the tissue fluids, and of other substances. They also form a sort of sieve for the penetration of substances soluble in fat, especially of those which dissolve more readily in lipoids than in water and aqueous albumin-colloids. The action of narcotic drugs stands in close relation with this solubility in lipoids. It may also be assumed that the functions of the lipoids may, within certain limits, be modified by their different chemical construction and solubility in the body juices, as well as by reciprocal solution. For it is known that the solubility of the best known lipoids, lecithin and cholesterin, may be altered in other fluids by mixing the two substances. Erla ndsen found that lecithin, which by itself is insoluble in acetone, became soluble to a slight degree in the presence of cholesterin. It must further be taken into consideration that the lecithin of the organism includes a large number of similarly constructed substances, which occur in mixtures in various proportions, and on account of the varying concentrations of salt solutions are differently influenced and precipitated or redissolved.

The permeability for albumins and inorganic (calcium, alkali and phosphoric acid) salts of the semi-permeable membranes formed by the lipoids, which is confirmed by the fact that the organic lipoids contain inorganic salts of this kind, facilitates the perception of the electrical processes which, in the opinion of various observers, take place in the cell.. Thus Höber and Nernst have developed theories which are intended to explain the connection between galvanic processes in the organ tissues and the stimulation of nerve activity.

The physiological processes which take place in the cells between lecithin and narcotic drugs are of great pharmaceutical interest. Harlen and von Bibra considered the narcotic action of ether and chloroform to be due to the liberation of fat by these drugs in the cells of the brain. Hermann assumed that the narcotic drugs attacked the lecithins and cholesterins of the ganglion cells. H. Meyer came nearer to the truth when he ascertained that the action of a narcotic drug was the more powerful the more readily it dissolved in lipoids and the less readily it was soluble in water. This was also confirmed by Overton. In his opinion the narcotic drugs pass into those components of the cell which contain

cholesterin and lecithin, and alter their physical condition in such a way as to disturb their functions, or to act injuriously upon the functions of other components of the cells. This alteration of function very probably depends upon a sort of anchoring of the narcotic to the lipoids, the bond being weakened by the introduction of other lipoids. This at least follows from Nerkings experiments. This observer administered to animals simultaneously intravenous injections of lecithin and urethane and found that the usual prompt action of urethane remained absent. He concluded that urethane, injected simultaneously with the lecithin, became anchored to the latter and was thus unable to enter into reciprocal action with the lipoids of the brain. Further experiments with ether, chloroform, morphine, scopolamine, novocaine, tropacocaine and stovaine gave a similar result. The subcutaneous, intravenous and intraperitoneal injection of these narcotics, applied simultaneously with lecithin, always caused an earlier return to consciousness, or the earlier reappearance of sensation. Similarly, animals which had previously received an injection of lecithin required a larger dose of the narcotic than those which had not previously undergone lecithin treatment. These results justify the conclusion that lecithin injections might be employed for human beings also, in order to shorten the period of narcosis or as a prophylactic against its troublesome secondary effects. For experiments of this nature subcutaneous injections of aqueous emulsions of lecithin or intravenous injections of lecithin-sodium chloride emulsions are suitable.

The part played by lecithin in haemolysis by poisons is also of physiological significance. In 1902 Flexner and Noguchi made the observation that blood corpuscles, which had been completely freed from the adherent serum by washing with physiological salt solution, were not dissolved by snake venom. They assumed that a substance was present in the blood serum which played the part of activator of the amboceptors of the snake venom, and this was later experimentally demonstrated by Kyes. According to Kyes, cobra venom which is inactive towards various kinds of blood immediately assumes haemolytic properties on the addition of lecithin. If cobra venom occasionally causes solution of blood corpuscles in spite of the absence of serum, it is due, according to Kyes and Sachs, to the lecithin contained in the blood corpuscles; and this occurs more readily the more loosely the lecithin is bound to

the blood corpuscle or to the molecule of protoplasm. The communications of Abderhalden and le Count show that the activating properties of lecithin may be arrested by cholesterol.

Finally, the relationship existing between the action of lecithin and that of Röntgen rays or radium rays has gained the consideration of physiologists. Reference may be made to the communications on this subject by Schwarz, Werner, Exner, Sywek, Neuberg, Wohlgemuth and Hoffmann.

### The Importance of Lecithin in Metabolism and Nutrition.

After the favourable effect of lecithin upon phosphorus metabolism and upon nitrogen metabolism had been established, first by Selenski and later by Serono and Charrin, Desgréz and Zaky, experimenting on animals, proved that feeding with lecithin leads to a lasting retention of phosphorus. According to their observations, phosphorus is used for bone-formation and for building up the brain; they were also able to prove that after feeding with lecithin the amount of lecithin in the brain was appreciably increased. The favourable influence exerted by lecithin upon metabolism in general and upon retention of phosphorus in particular, led the two observers to undertake more exhaustive observations on guinea-pigs, in which they found that it was not the glycerophosphoric acid, but the choline which diminished the excretion of phosphorus and causes an increase in the body-weight, e. g., that the action of lecithin depends upon its basic components. Hatai was able to confirm the favourable influence exerted by lecithin upon growth. He treated white rats belonging to one and the same brood, some with lecithin and some without, and obtained the surprising result that the animals treated with lecithin thrived considerably better, indeed they increased in body-weight by 60 p. c. more than the other animals. Internal administration brought about the best results, but better growth of the animals was also observed after subcutaneous administration.

Danilewski noticed that tadpoles grew with extraordinary rapidity under the influence of lecithin, and he therefore tried the drug in young dogs. He found that the subcutaneous and internal administration of lecithin is a great

incentive to bodily growth, improvement of the blood and increase of the brain, which he explains as an acceleration of the bioplastic, morphogenous processes. He observed especially that the dogs treated with lecithin appeared much more lively, more intelligent and physically stronger than the control animals. For his experiments he employed an emulsion of lecithin in physiological salt solution, of which he injected doses of 0·02 to 0·05 gramme of lecithin under the skin of the abdomen, or gave double this dose by mouth. In further experiments on the blood-forming properties of the spleen and the bone marrow, Danilewski and Selenski arrived at the conclusion that lecithin plays an important part in the haemopoietic processes which take place in these organs. This assumption gains in probability when it is borne in mind that lecithin is capable of adsorbing and binding in the organism various substances of importance in the vital process, such as albumins, sugars, salts, ferments, etc., substances which for their part are readily decomposed into their components.

An insight into the relations which exist in metabolism under the coöperation of lecithin is also furnished by the results of the investigations of Franchini, Massaciu, Buchmann, Zuntz, Yoshimoto and Slowtzoff. According to Franchini, feeding rabbits on lecithin increases the lecithin content especially in the liver, less in the muscles and not at all in the brain. The increase in the lecithin content of the liver remains for some time, even after the ingestion of lecithin has been discontinued. The discovery of the author that only very little lecithin is excreted in the faeces tallies with other statements which have been mentioned above. Franchini also confirmed the observation that during lecithin administration an increased amount of glycerophosphoric acid is found in the muscles and in the liver. He also found a slight increase of this acid in the urine, though this may have been first formed from lecithin in the urine, for lecithin is a somewhat labile substance. The fact that no choline could be found in the urine is, however, not in favour of this view.

The choline which is split off from the lecithin during metabolism is, according to the author, further broken down and oxidised in the organism, and appears as formic acid in the urine. Another hypothesis which has not yet been proved has been suggested by Löw. He assumes that lecithin acts in metabolism as a fat-carrier, the fatty acids being split off

from the molecule and then replaced by new ones. Part of the lecithin-phosphorus is, according to Yoshimoto and Buchmann, kept back for some time in the organism and is most probably only very gradually excreted. Besides retention of phosphorus, Yoshimoto, Zuntz and Slowtzoff also found retention of nitrogen, which was not always accompanied by an increase in body-weight. Völtz and Massaciu also observed an increase in the albumin content after feeding dogs and guinea-pigs on lecithin, whereas Rogozinski was unable to demonstrate either an increase in nitrogen or phosphorus.

These experiments on animals, the results of which are in part contradictory, have long been rendered perfectly clear by means of the practical employment of lecithin in man. The investigations on metabolism carried out by Cronheim and Müller on several children (under a year old) are interesting. On feeding with children's meal (consisting of skim milk powder, oatmeal and sugar) and administering lecithin, the nitrogen of the food was better assimilated and retained by the body than was the case when lecithin was not administered simultaneously. In the former case the nitrogen retention amounted to 19 to 28 p. c., in the latter case only to 2 to 24 p. c. On the other hand, as regards phosphorus retention, food containing lecithin showed no advantages, nor could any influence on fat and carbohydrate metabolism be observed. Calcium and magnesium salts were, however, held back by the lecithin, which is a point in favour of increased bone-formation. The older the children, the more evident was the favourable influence of lecithin. This phenomenon is perhaps due to the fact that the body of the suckling contains, according to Siwertzeff, a large store of lecithin, which is gradually used up in the course of the first 4 to 5 months of life. Thus, children under 5 months of age are so richly supplied with lecithin that a further supply becomes superfluous and cannot be utilised. The utility of the drug really first becomes apparent when the store of lecithin has been exhausted.

Recent experiments by Cronheim show that lecithin is not only valuable during growth, but is also of value to adults. A fully developed individual requires a certain amount of lecithin for the maintenance of normal metabolism. It is therefore justifiable to assume that the drug is as beneficial for adults as for children.

Massaciu carried out the following metabolism experiment on a man: he was first given meat and no lecithin, in the second experimental period he received roborat containing lecithin, and in the third period he was given both meat and lecithin. The assimilation of nitrogen was increased threefold in the second period as compared with the first, the nitrogen being better utilised in the intestine. The same occurred in the third period. This furnished a further proof of the nitrogen-sparing power of lecithin. The author also observed retention of phosphorus during lecithin administration. Marfori's results are in agreement with this; he found that egg-lecithin, when subcutaneously applied, furnished the organism with phosphorus capable of being assimilated.

Moricheau Beauchamp experimented on himself and on a medical student and found a nitrogen-sparing and phosphorus-sparing action. The author administered 0.5 to 1 grammie of lecithin a day and found after 4 days that he had gained in energy and that his weight had increased by 900 grammes. In the urine he found a decrease of nitrogen, urea, phosphoric acid and xanthin bodies.

The value of lecithin in nutrition is also shown in a paper by Usuki. The author found in experiments on dogs that lecithin has a favourable influence on the saponification of neutral fat, and that it thus accelerates the digestion of fat. As regards digestion in general, the only doubtful point is whether lecithin exerts a favourable or a harmful influence upon it, or upon the digestive ferments. This point has not yet been settled. Certain conclusions may, however, be drawn from the communications of Hewlett, Fürth, Schütz, Küttnér, Kalaboukoff and Terroine. Fürth and Schütz found that bile has the power of augmenting the action of the fat-splitting and albumin-splitting pancreatic ferments, which they consider to be closely connected with the presence of bile salts. Nencki had previously made a similar observation. Hewlett, on the other hand, considered the favourable influence upon these ferments to be due to the lecithin content of bile; Fürth and Schütz were only able to confirm this in the case of an alcoholic solution of lecithin. Küttnér attempted to test more carefully the influence of lecithin upon the digestive ferments; he came to the conclusion that definite additions of lecithin sometimes hasten and sometimes delay the enzyme action of gastric or pancreatic juice. He was, however, unable to

offer a reliable explanation of the matter. Kalaboukoff and Terroine have expressed the decided opinion that diastatic ferments are not influenced by lecithin. The results of their investigations are as follows: "The addition of lecithin to pancreatic juice never hastens its decomposing action on monobutyryl; it hastens very slightly the action upon oil, but only in relatively high concentrations. — The lipolytic action of glycerin extracts of gastric mucous membrane remains unaltered by the addition of lecithin; intestinal lipase is unaltered by the addition of lecithin. — The addition of lecithin has no effect upon the rapidity of starch hydrolysis, of digestion of casein and coagulated albumin, or upon the coagulation of milk and pancreatic juice." These results throw doubt upon Hewlett's view mentioned above. The communications of Bang, Wohlgemuth, Lapidus and Starkenstein also show that lecithin does not possess the accelerating action assigned to it by Hewlett.

Slowtzoff, as a result of his lecithin experiments on man, came to the conclusion that lecithin occasioned retention of nitrogen, accompanied by a diminution of sulphuric acid excretion in the urine. He considers this to be related to the decomposition of albuminous bodies, and concludes that what occurs is retention of albumin and not retention of other nitrogenous products (extractives). In his opinion, the assimilation of albumin runs parallel with the assimilation of phosphoric acid and the diminution of the albuminous substances. This phenomenon shows that lecithin promotes the organisation of albumin, e. g., its transformation into tissue-albumin. This transition of absorbed into organised albumin must, according to U mikoff and Slowtzoff, be considered as being due to the addition to the albumin of phosphoric acid and xanthin bodies. Thus, according to Slowtzoff, lecithin acts favourably upon this organisation, and it is comprehensible for the increased assimilation of albumin to be accompanied by the retention of xanthin bodies and of phosphoric acid.

### Lecithin in Therapy.

Before considering the employment and the therapeutic use of lecithin, we would point out that in certain pathological conditions of the organism and in certain organs, an

accumulation or a diminution of lecithin may occur. This phenomenon is merely referred to here; it need not necessarily be taken into consideration in the therapeutic administration of lecithin in individual cases. No experiences have come to my knowledge in which the abnormal accumulation of lecithin in any organ (in so far as this can be judged *in vivo*) has suggested a contra-indication. It is justifiable to consider the drug indicated in those diseases in which a considerable loss of lecithin has been established. In any case, according to the present position of lecithin research, it must be borne in mind that the lecithins play an important part in many and perhaps even in all pathological processes. This is made evident by the part played by the lipoids in tabes and general paralysis. Reference will be made to this below.

Balthazard was the first to draw attention to variations in the lecithin content of the liver under normal and pathological conditions. He found that in animals and in man the amount of lecithin in the liver was greatly increased in toxic conditions, as for example in tuberculosis, diphtheria, phosphorus poisoning and typhoid, and also in auto-intoxications (inanition and uræmia). Thus a considerable increase in the amount of lecithin was noticed in the liver (which had undergone fatty degeneration) of a man who had died from pulmonary tuberculosis, and also in the livers of fattened geese. A liver weighing 1160 grammes contained 9.8 p. c. of lecithin, while one weighing 850 grammes contained as much as 23 p. c. of lecithin. The author considers the increase in lecithin to be due partly to the destruction of liver cells and partly to the decomposition of leucocytes, the lecithin of which is deposited in the liver and there held fast.

Mott and Halliburton state that in tabes and progressive paralysis, in combined and disseminated sclerosis, alcoholic polyneuritis and beri-beri, lecithin is set free by the disintegration of the spinal cord; that it is further broken down and appears in the blood and the cerebro-spinal fluid in the form of one of its products of decomposition, choline. Besides being present in organic diseases of the central nervous system, choline was also found by Donath in the cerebro-spinal fluid of epileptics; this points to the conclusion that in epilepsy also there is a destruction of nerve-substance with liberation of lecithin.

The behaviour of lecithin in bone marrow under pathological conditions was studied by Glikin and Peritz. As has been mentioned above, human beings (and mammals) are born with a large supply of lecithin; this decreases rapidly at first and in time more slowly, but it never altogether disappears from the bone marrow. Glikin found that the fat of the bone marrow of a man aged 34 contained 3.3 p. c. of lecithin, that of a man aged 70 contained 2.3 p. c., that of a man aged 88 contained 1.8 p. c. of lecithin. Thus, under normal conditions, lecithin is apparently a component of bone marrow. In paralytic processes the authors find a difference. In a tabetic aged 40, and in a man aged 36 suffering from paralytic dementia, only traces of lecithin were found in the tibiae; in other similar cases of the same age lecithin was altogether absent. From this it is evident that in paralytics the composition of the bone marrow may undergo a change, which takes the form of partial or total disappearance of lecithin. Lipoid-iron disappears with the lecithin. No investigations have as yet been made of the causal relations between the disappearance of lecithin and the existence of paralysis.

The investigations carried out by Glikin on the blood of a patient suffering from polycythaemia are of interest. They were prompted by a communication by Loewy, who had found a considerable increase of iron in the blood in polycythaemia. Glikin also found a considerable increase in lecithin. Whereas, according to Abderhalden, blood contains 0.2 to 0.3 p. c. of lecithin, the author found 0.5 p. c. in the blood of polycythaemic patients. As polycythaemia is accompanied by a considerable increase in the red blood corpuscles, Glikin thus proved that with an increase of cells, in this case of blood cells, the amount of lecithin is correspondingly increased.

As regards the lecithin found in ascitic fluid by Mackenzie Wallis and Schölberg, the pathological significance of this phenomenon has not yet been explained. In the pseudo-chylous fluids investigated by them, lecithin was present in the form of an adsorption compound with globulin. The presence of lecithin gives a milky appearance to the fluid and keeps it fresh; ascitic fluid, from which the lecithin has been removed, immediately begins to putrefy. This antiseptic property of lecithin, which is of course only relative, was also observed by Renshaw and Atkins; they found that lecithin had on the whole a slightly retarding action on growth in cul-

tures of *coli* bacillus, typhoid bacillus and other bacteria. It is definitely shown in the investigations of H. Ehrlich, Noguchi, Abderhalden and le Count, Jagic, von Eisler, Dautwitz, Pascucci, Bang, Raubitschek, Landsteiner, Friedemann, Kyes and Sachs that lipoids take part in the phenomena of bactericidal action, haemolysis and cytolysis, either by themselves or in combination with albuminous bodies. According to Pick and Schwarz, on the other hand, the function of lipoids consists chiefly in the part they take in the course of specific immune reactions, more especially through their physico-chemical properties, e. g., through adsorption, effect on surface tension, alteration of the solvent, etc.

The rôle of lipoids in pathological processes was first elucidated to some extent by Overton and Meyer. They showed that an active narcotic, as for example chloroform, must be soluble in lipoids, which indeed is true for chloroform; that a parallel exists between the action of the narcotic and its solubility in oils; and that narcotics may be arranged in a progressive scale of potency according to their greater solubility in oils or in water. The solubility of the narcotics in lipoids and their capability or endeavour to combine with the organ lipoids is demonstrated by the fact that after narcosis they are found in the brain, the chief seat of lipoids. The experiences of Nerkling and Reicher are in agreement with Overton's observation; according to them, the introduction of lecithin into the circulation eliminates the effects of narcosis, and the lipoids can also be extracted from the organs by means of narcotics.

The results of the studies of Kyes and Sachs also furnish an important indication; these show that lecithin can form compounds with toxins, the prototype of which is the toxo-lecithide of cobra venom described by these observers. As regards the haemolytic action of these toxo-lecithides or toxo-lipoids, reference should be made to the communications of the two authors mentioned and to the publications of Pascucci, Bang, Friedemann, Abderhalden and le Count, and others. The fixing of toxins by lecithins is probably of the highest importance for the pathology and therapy of lecithin. Thus, Wassermann was the first to point out that the poison of tetanus is fixed by a brain substance, and Landsteiner considers this brain substance

to be protagon (a lecith-albumin). Other toxins probably behave in a similar way to tetanus toxin, as was shown for example by Calmette for the toxin of tuberculosis, and by Porges and Meyer for the toxin of syphilis.

It stands to reason that a body which, as has been described, is of such high significance for the life of the cell, for nutrition and metabolism and for pathological processes, should claim much attention in therapy. The therapeutic experiences which have been recorded in the literature are described in the following notes, arranged according to indications.

#### Anæmia and Chlorosis.

Since Danilewski and Serono carried out their classic researches, no doubt can be entertained regarding the high value of lecithin in the therapy of anæmia and chlorosis. Serono observed that the number of red blood corpuscles in man and animals was doubled under the influence of lecithin injections, and he pointed out that lecithin could be employed in diseases of the blood. The author also noticed that the improvement in the condition of the blood was accompanied by increase of appetite and of digestive activity, in consequence of which the body-weight was increased and the general health improved. This beneficial action of lecithin is confirmed in the communications of Goliner, C. Lewin, F. Levy, Sicuriani, Bergell and Braunstein, V. Brutti, G. Cicionardi and J. Nerking. Most of the authors mentioned have also used lecithin in chlorosis with excellent results. According to Brutti, it is not only beneficial in the asthenia occurring in chlorosis, but is also capable of markedly increasing the percentage of blood corpuscles and of haemoglobin in the blood. The experience of various authors that lecithin gives good results where iron treatment has failed is of special importance for the treatment of anæmia and chlorosis. Of course, lecithin may be administered in combination with iron preparations, as has been suggested by Lewin.

The action of lecithin is not due to the minute amount of iron which even the purest lecithin contains, but to the beneficial influence of the drug on the condition of the blood and on metabolism. It is therefore not improbable that lecithin will also prove of service in pernicious anæmia, especi-

ally when combined with other suitable drugs, such as arsenic and iron. It is not impossible that part of the success obtained by various observers in medullary therapy of pernicious anaemia has been due to the lecithin content of fresh bone marrow (compare Merck's Report 1908, p. 72). As far as I know, no special experiments with lecithin in pernicious anaemia have as yet been recorded.

It has been supposed that lecithin acts more or less as an iron-carrier in chlorosis, and that it fixes the iron in the organism and delivers it in an assimilable form to the places where it is suitably utilised. This assumption is founded on the experience of various observers, such as Thudichum, Strecker and Erlandsen, that lecithin is capable of forming crystalline compounds with metals.

#### Athrepsia.

Muggia was the first to draw attention to the value of lecithin in infantile atrophy, in which he obtained good results with the preparation. Narbret confirmed the action of lecithin in the athrepsia of children, even in the most hopeless cases. According to the author, intramuscular injections of 1 c. c. of lecithin emulsion (on alternate days) soon brought about normal stools, the general health and the appetite improved and the body-weight was markedly increased. In less severe cases the internal administration of lecithin is efficient; in breast-fed children indeed, if there be no immediate danger, it may be well to administer the lecithin in suitable doses to the mother, for it has been proved that the drug enriches the mother's milk in lecithin.

This treatment might prove of value in the treatment of sucklings in general, when the growth of the infants is unsatisfactory. Under normal conditions breast-fed children will obtain sufficient lecithin in the mother's milk, for, as Burrow has shown, mother's milk is comparatively rich in lecithin. But in abnormal cases, when this does not occur, or when the amount of lecithin in the infant organism, together with that taken in with the milk, is insufficient, it will be wise to follow Lanceraux' suggestion, namely to administer lecithin to the mother and thus attempt to increase the percentage of lecithin in the milk, whereby the mother is strengthened at the same time.

### Diabetes mellitus.

The administration of lecithin only comes into consideration in diabetes when treatment is required for loss of strength and for debility, which may occur in consequence of abnormal conditions of the blood. Thus Adler has shown that in diabetic lipæmia much cholesterin, but only very little lecithin is present in the blood; and that therefore the view held by Klempner and Umber, namely that lipoidæmia always occurs with lipæmia, is fallacious. In two cases of diabetes, both showing much acidosis, he found in 100 grammes of blood extract with a total amount of 92·5 grammes of fat 7 grammes of cholesterin and 0·5 grammes of lecithin; and in another case a high percentage of cholesterin and only traces of lecithin. Thus, lecithin therapy is apparently not without prospect of success in cases of debility and malnutrition due to diabetes, especially if the drug be applied subcutaneously, for according to Stassano and Billon, lecithin is eagerly absorbed by the leucocytes. Lanceriaux, Serono and Huchard, indeed, obtained highly satisfactory results in cases of rapid emaciation by the administration of internal and subcutaneous daily doses of 0·2 to 1·0 gramme; the general health improved and there was an increase in weight. Erben's results, on the other hand, were negative. To diabetics, whose blood examination showed that the erythrocytic substance was poor in lecithin, he administered up to 6 grammes of lecithin a day, but he observed no marked improvement in either slight or severe cases. It is possible that there existed in his cases a primary developmental anomaly of the blood cells, which manifested itself in the loss of power of the erythrocytes to take up lecithin and to use it in a normal way. The contradictory results obtained by these two authors can only be cleared up by further investigations.

### Mental Overstrain.

It is not merely an accidental occurrence that the brain is the organ of the human organism richest in lecithin; rather is this fact due to the nature of the brain and to its activity. Psychologists have for a long time made use of brain substance on this account in organotherapy (compare Cerebrum siccum, Merck's Report 1908, pages 8 to 10) in order to supply to the human brain those substances which it requires in order to carry out its normal functions and to relieve morbid

symptoms. Since organically bound phosphorus is known to be an important factor in cerebral activity, we may assume that it is upon lecithin that the psychic functions of the brain depend. Further, the therapeutic success of the use of lecithin justifies us in assuming, even without the difficult clinical proof, that the expenditure of brain substance, which is accompanied by functional weakness and exhaustion and fatigue of the brain, with consequent partial failure of mental activity, is chiefly due to the undue expenditure of lecithin. According to Fürst, the loss of lecithin accompanying cerebral activity, which becomes manifest by increased mental exertion, may be compensated on the one hand by rest and recovery of the brain, and on the other hand by increased nutrition of the organ, which may be effected by the administration of lecithin. For normal work the brain obtains a sufficient amount of lecithin from the blood; but if an abnormal amount of work is to be done, a greater amount of lecithin must be introduced into the blood in order that it may be carried to the brain. According to this author, it makes little difference whether the drug be introduced by mouth or subcutaneously; internal administration will usually be preferred. Children may be given 0.05 grammes and adults 0.1 grammes of lecithin three times a day.

The practical experiments carried out by Fürst on school children and adults (students, scholars, artists, etc.) gave proof of the high value of the preparation in mental fatigue. In persons of all ages, suffering from receptive, productive or speculative mental overstrain and consequent fatigued cerebral function, he observed a beneficial effect of lecithin, even after only 4 to 6 weeks' administration. The state of nutrition and the condition of the blood were improved and this was followed by an improvement in the cerebral functions, both as regards intensity and durability. The capacity for clear thinking, comprehension and judgment were enhanced.

At the end of his paper, Fürst therefore rightly says:

"The same biological laws apply to the economy of the brain as to other organs, except that in the brain there is the added necessity for constant lecithin equilibrium. Increased consumption of phosphorus must be met by increased introduction of phosphorus. As it is now possible to effect an enrichment with lecithin in a very simple manner, we have advanced a step towards the removal of subnormal nutritive

conditions of the brain. For in these cases the action of excitants is only transitory, and at the same time they increase tissue consumption; whereas a body like lecithin combines a nourishing with a stimulating action."

Fürst's results are partly confirmed by Bain. He also used lecithin with benefit in over-exertion and nervous exhaustion, and also in insomnia (of neurasthenics).

#### Heart Affections.

In order to improve the conditions of nutrition and strength in heart affections without causing over-feeding, Mendelsohn recommended the systematic and continuous administration of lecithin, as well as the usual treatment. In an example quoted by the author it is seen that lecithin may occasionally be of service where cardiac and circulatory treatment have failed. Thus, in an old man he had used digitalis and sparteine without benefit, while injections of 0.1 gramm of lecithin administered on alternate days maintained the cardiac activity for months. Like Nerking, Mendelsohn emphasises the necessity of using pure lecithin in order to obtain good results. He often observed that pure lecithin was very beneficial in cardiac affections, while food containing lecithin was without effect, even on resorting to over-feeding. Mendelsohn's observation that hen's eggs cannot serve as a substitute for pure lecithin is of interest. Thus a neurasthenic took 6 to 12 eggs a day for months without benefit, while doses of 0.25 gramm of pure lecithin soon brought about an improvement. The author considers this to be due to the fact that pure lecithin is not attacked by gastric and pancreatic secretions and is thus enabled to act better. Dor had previously observed that eggs did not form a substitute for lecithin.

#### Menstrual Disturbances.

H. de Wilczinski pointed out that lecithin could under certain conditions be used with benefit as an anti-menorrhoeic. As in certain diseases, such as incipient pulmonary tuberculosis and chlorosis, great loss of blood, as is caused by too frequent menstruation, aggravates the anaemia and thus diminishes the resistive power of the patients, the author attempted to regulate the occurrence of menstruation by the administration of lecithin. He began the treatment in the intervals between the menstrual periods and gave

0·1 to 0·2 grammes of lecithin 3 times a day for a fortnight. Distinct benefit is said to be apparent even from the first series of administrations. Thus, in one case, in which the menses recurred every fortnight, he obtained a delay of first a week and then a fortnight in the bleeding, so that menstruation returned to normal. In regular but too profuse menstruation, its commencement is said to be postponed for 1 to 2 weeks by the use of lecithin, if delay be desirable on account of too great loss of blood. A lasting result can only be achieved by long continued use of lecithin.

### Migraine.

Schottin expressed the view that migraine was due to poverty in phosphorus of the cortical centres. In one case he observed that the first attack of migraine was brought on by anger. This fact and the circumstance that the attack which had been called forth by a process of the intellect was only completely relieved by sleep, demonstrate in his opinion that the seat of the disease is in the cerebral cortex. As spasmophilia of children, which is due to abnormal irritability of the child's brain, is known to be improved by the administration of phosphorus, the author tried phosphorus medication for the migraine of older persons, prescribing it in the form of lecithin dissolved in cod-liver oil. The medication is said to have proved beneficial in several cases. But, according to Schottin, a lasting result is not obtained, the effect depending rather upon renewed medication.

### Nervous Diseases.

Lecithin therapy is of special significance in the treatment of nervous diseases. As lecithin is a highly important component of the brain and nerves, which is never absent under normal conditions, and which is used up, as Gautier has shown, through the activity of these organs, the obvious indication is to provide for the restitution of this substance. Otherwise the continuous loss of lecithin would lead to transitory or permanent injury to the nervous system. Although lecithin is regularly introduced into the organism in the food, it is usually insufficient in amount, and may be present in the food in a form or combination which is absorbed with difficulty in the digestive tract. We know, for example, that lecithin is present in the grains of corn chiefly in the

form of albumin compounds, from which it can with difficulty be isolated by chemical means. We may therefore assume that in the stomach and intestine the absorption of these bodies also takes place more slowly and less completely. This assumption is borne out by experience, for we know from Nerkings investigations that the action of pure and free lecithin is alone reliable. The success obtained by the use of really pure lecithin in the most varied nervous diseases therefore justifies the endeavour to use only the purest lecithin for therapeutic purposes.

Danilewski, acting upon the assumption that diseases of the nervous system are often caused by defective neoplastic restitution within the nerve substance, was the first who attempted to raise the disordered nerve tone by the administration of lecithin. He tried the drug on himself, taking doses of 0·2 to 0·3 gramme. The good result was shown by improved nutrition, increased self-reliance, resistive power and mental vigour. Gilbert and Fournier obtained equally good results in neurasthenia. They gave single doses of 0·1 to 0·5 gramme.

In a severe case of neurasthenia, accompanied by phosphaturia, Nerk ing gave a teaspoonful of lecithin chocolate 3 times a day; this led in the course of 3 months to the disappearance of phosphate excretion. The appearance of abnormally large amounts of phosphates in the urine is a phenomenon which may almost always be observed in mental overstrain, mental diseases and nervous disorders. Gautier stated, based on his investigations, that during nerve activity phosphoric acid is formed from lecithin and is excreted as such. On account of the appearance of large quantities of phosphoric acid in the urine, Martell draws the conclusion that a loss of lecithin takes place in the nerve centres. This furnishes a sufficient theoretical explanation of the satisfactory results obtained by these and other authors in nervous diseases. It follows from what has been said that lecithin must also act beneficially in mental overstrain. This was confirmed among others by Fürst who, by the administration of lecithin to children and adults, obtained an improvement in the cerebral functions and in the capacity for work. According to Massaciu, it stimulates the nervous system to increased capacity for work, and in comparison with those persons who are receiving no lecithin though taking the

same food, it increases nitrogen retention threefold, and causes a diminution of phosphates in the faeces by as much as 32 p. c.

In neurasthenia with cardiac weakness, J. Ferreira combined lecithin medication with camphor. For this purpose, a solution of 0·5 grammes of lecithin and 0·5 grammes of camphor in 10 c. c. of olive oil is used, of which 1 c. c. is injected subcutaneously, on alternate days in slight cases, and every day in severe cases.

Lecithin has further been found of great value in diseases of the spinal cord, general paralysis and in psychoses. The fact established by Glikin and Peritz that in tabes the bone marrow becomes poor in lecithin, pointed to the probability that lecithin medication would be of use. Lecithin has proved of value in many cases of tabes and general paralysis, as is evident from the communications of Hartenberg, Nerking and others. Nerking, for example, describes a case of severe tabes in a syphilitic subject, in whom the daily administration of 3 doses of one teaspoonful of lecithin chocolate produced an undoubted and lasting improvement in the general health, a gain in weight of 5 pounds and return of the appetite and energy. The same author also reports a case of hysteria in a woman aged 22, who also suffered from nervous palpitation, nervous gastric disturbances and anaemia. She had been treated for two years without effect with arsenic and other drugs; lecithin, combined with baths and galvanisation, caused a considerable increase in the haemoglobin content of the blood, increased the patient's capacity for work and enjoyment of life, while she gained 10 pounds in weight in three months. The communications of Serono, Coulombe, Brutti, Goliner, Sieffert, Moricheau and Beauchamp on the treatment of nervous diseases with lecithin are also most favourable.

#### Nicotine Amblyopia.

French observers have found a new field of usefulness for lecithin in visual disturbances, such as are occasionally caused by alkaloids. They found that lecithin is able to dissolve alkaloids and thus prevent amblyopia, and remove visual disturbances. Thus, in a recent case of nicotine amblyopia, Nuel obtained a surprisingly rapid recovery, such as he had never observed with the usual treatment. But, in his opinion, lecithin failed in chronic cases. De Waele, on

the other hand, also obtained good results in chronic cases. Strychnine proved but slightly efficacious. According to de Waele, lecithin may be given internally or subcutaneously, for which purpose lecithin emulsion Merck in ampoules is specially suitable, a form of administration which the author hails as an advance. The method was also used by Danis, with excellent results in two cases, with a good result in a third, and with an unsatisfactory result in another case.

#### Rickets and Scrofula.

In rickets, when accompanied by imperfect calcification of cartilage, increased absorption of bone and formation of osteitic tissue, lecithin therapy has long been of special interest. This is especially the case since Desgrez and Zaky proved that lecithin has an excellent effect upon bone-formation, probably on account of its content of readily absorbed phosphorus. The significance of lecithin in bone-formation is also dealt with in communications by Plimmer and Scott; they showed that the bones of the young animal, formed on hatching a hen's egg, obtain their phosphorus solely from the lecithin contained in the egg yolk. We know, besides, that the total phosphorus of the bony skeleton of man and beast is originally derived from vegetable foods, in which the phosphatides are apparently present in sufficient quantity and in a form suitable for supplying the organism with the necessary amount of phosphorus. I need hardly point out the universally recognised fact that phosphorus, or phosphoric acid, exerts a favourable influence on the formation and growth of bones, that it is indeed an essential factor in bone-formation. Another almost universally recognised fact is that the human organism absorbs inorganic phosphorus salts with difficulty and slowly or not at all, whereas organic phosphorus compounds, such as glycerophosphoric acid and lecithin, which is chemically related to it, are comparatively readily and completely absorbed and are then excreted as phosphates. Reference may also be made to the results of Heubner's investigations, according to which absence of phosphorus has a disturbing effect upon the growth of bone, while lecithin-phosphorus alone suffices to maintain growth.

Communications by Hartenberg, Carrière, Golliner, Sieffert and Bain deal with the therapeutic use of lecithin in rickets. They are wholly favourable.

The first to give lecithin a serious trial in rickets was Carrière, who describes 5 cases. He administered the drug in cod-liver oil (2·05:500·0) with meals, the children receiving 1 to 4 tablespoonfuls according to age, i. e., daily doses of 0·05 to 0·2 gramme ( $\frac{3}{4}$ —3 grains). All the cases were cured by this medication without relapse within 4 to 6 months. The results are of special value, as the physician is now able to use lecithin-cod-liver oil, a preparation which has all the advantages of phosphorus without any of its disadvantages, instead of phosphorated oil the use of which is not free from danger. Lecithin chocolate tablets are perhaps more suitable for children, as they are readily taken. (Compare page 40.)

Sieffert and Sicuriani also obtained satisfactory results with lecithin in scrofula.

#### Debility.

A special indication for lecithin is given by debility such as results from deficient nutrition, in convalescence from debilitating infective diseases, e. g., typhoid, influenza, etc., in old age, in consequence of sexual excess, after childbirth, and in a series of diseases, some of which have been mentioned above.

The physiological investigations of Danilewski, Serono, Stassano and Billon, Desrez and Zaky clearly show that lecithin improves the condition of the blood, increases the resistive power of the elements of the blood, has a favourable influence upon leucocytosis and promotes the exchange of nitrogen. Thus a proof is furnished of the utility and the benefit to be derived from the preparation in all conditions of debility. This has been confirmed in practice; and recently, since I have placed a really pure lecithin on the market, I have received an increasing number of favourable reports as to the high value of this drug.

According to the observations of Ariés, Riez, de Diego and others, lecithin appears to be of special benefit in various troubles of old age. In their experience, it shortens convalescence after acute infective diseases, removes disturbances of nutrition, and, to a certain extent, furnishes the debilitated organism with new vitality. Sieffert's communications agree with the results of these authors; he gave lecithin with good effect to feeble old men, and to persons debilitated through excesses. He preferred internal administration, whereas J. Ferreira prescribed the subcutaneous use of the remedy. In de-

bilitated conditions, such as those following typhoid and influenza, which are accompanied by cardiac weakness, he recommends a combination with camphor. Injections of oily solutions are suitable for this purpose, for both lecithin and camphor dissolve in oil with comparative readiness. A solution of 0·5 grammie ( $7\frac{1}{2}$  grains) of lecithin and 0·5 grammie ( $7\frac{1}{2}$  grains) of camphor in 10 c. c. ( $\frac{1}{3}$  oz) of olive oil is used, of which 1 c. c. is administered subcutaneously, in slight cases on alternate days and in severe cases every day. (Compare p. 33.) According to Sicuriani, lecithin is useful in the cachexia of malaria.

Recent clinical experiments by Bain have added to our knowledge of the value of lecithin. He declares the preparation to be a valuable remedy in the treatment of anaemia and debility.

J. Nerking, who has done much good work in connection with lecithin research, utters a special warning against the employment of inferior commercial preparations of lecithin. In order that the valuable therapeutic properties of lecithin may actually take effect, it is, in his opinion, absolutely necessary to use pure lecithin, and above all it must be free from cholesterol, which has a diametrically opposite effect. It must also be free from fatty acids, as lecithin does not keep so well when they are present. Nor is it a matter of indifference whether the lecithin be prepared from vegetable substances or from yolk of egg; vegetable lecithin is with difficulty freed from impurities and is moreover probably not identical with animal lecithin. The author regards a commercial preparation which contains 70 p. c. of pure lecithin as a highly impure lecithin, to which no physiological action can be imputed. Nor has lecithalalbumin, according to Nerking, the same therapeutic efficacy as pure lecithin; indeed, he considers the lecithalalbumins to be valueless as substitutes for lecithin, because the lecithalalbumin of the human organism has a special variety of albumin as a component, which it builds up out of the food and which combines with the lecithin introduced into the body.

Nerking, as a result of his experiments, considers Lecithin puriss. Merck to be the best lecithin obtainable at the present time, and for this reason he particularly recommends its use. He used it, or the preparations made from it, viz., lecithin chocolate, lecithin chocolate tablets and lecithin emul-

sion (compare p. 40) in the treatment of a series of cases, especially of anaemia, chlorosis, neurasthenia, hysteria, tabes, etc., and always obtained marked improvement. He quotes the following cases from his records as being especially instructive:

1. A lady, aged 22, suffering from anaemia, severe hysterical troubles, nervous palpitation and gastric disturbances, had for two years been treated in vain with a great variety of drugs, including arsenic and iron. The author prescribed 1 teaspoonful of lecithin chocolate Merck 3 times a day, together with galvanism and baths. In 4 weeks the percentage of haemoglobin had risen from 70 to 92, and in 3 months she had gained 10 pounds in weight. The patient felt brisker, readier for work and better able to enjoy life.

2. A man, aged 52, in a very bad state of health, suffering from tabes on a syphilitic basis, was given 1 teaspoonful of lecithin chocolate Merck 3 times a day; there was permanent improvement in the general health, return of appetite and energy and a gain of 5 pounds in weight.

3. A neurasthenic, aged 38, with severe phosphaturia, received the same amount of lecithin. The phosphaturia gradually diminished and in 3 months had disappeared.

#### Metabolic Diseases, Intestinal Auto-intoxications.

Liebermann, in an interesting paper, has explained the significance of lecithin in hydrochloric acid secretion of the stomach. From this it appears that a lecithin compound (lecithalalbumin), existing in the gastric mucous membrane, plays an important part in the formation of sodium carbonate and hydrochloric acid from sodium chloride. Important as these conclusions may be physiologically (for they give us a glance into the physiological work which, among other things, is done by lecithin in the organism), yet no direct inference can be drawn from them regarding the therapeutic employment of lecithin in gastric disease; though others have done so. It would first be necessary to prove that by the administration of lecithin the percentage of lecithalalbumin in the gastric mucous membrane could be increased and that thus the gastric secretion could be influenced in a manner favourable for digestion. Experiments of this nature, or indeed any investigations which explain the direct value of lecithin in gastric

disorders have not, to my knowledge, been carried out. Nevertheless, an indirect favourable influence on digestive disorders resulting from defective gastric secretion is quite conceivable, for there is no doubt as to the therapeutic value of lecithin in metabolic diseases. (Compare the paragraph on Diabetes p. 28.)

According to Voet, lecithin has proved of service in gastro-intestinal auto-intoxications. On administration of the drug, with food rich in carbohydrates, together with intestinal irrigation and hydropathic measures, the author observed a diminution of the toxic symptoms and of the foetidity of the stools, and the disappearance of the paired ethylsulphuric acids from the urine. These symptoms, according to Voet, appear when the function of the liver is deficient, for in auto-intoxication the latter usually supplies the detoxicating substances.

### Tuberculosis.

Communications by Claude and Zaky, Golinier, Sicuriani, Bernheim and Dieupart, Lancereaux and Paulesco, Moricheau and Beauchamp, Gilbert and Fournir deal with the therapeutic value of lecithin in tuberculosis. Claude and Zaky succeeded in actually demonstrating the beneficial action of lecithin on animals infected with tuberculosis. The animals treated with lecithin always survived the control animals, the morbid process assumed a benign form, remaining stationary and following a subacute course of a bronchopneumonic type, ending in sclerosis. The authors also experimented upon 20 tuberculous patients. In almost half the cases they observed improvement in the morbid condition after the employment of lecithin. In their experience, a good result may be expected in the first and second stages of the disease, but it is uncertain in the presence of cavities. Lecithin fails in acute cases, though it usually effects a less rapid decline. Lancereaux also obtained good results with lecithin medication in early pulmonary tuberculosis and in tuberculosis of bones. He gave 0·2 to 0·5 grammé ( $3-7\frac{1}{2}$  grains) a day. According to Moricheau and Beauchamp, the action of lecithin is very satisfactory especially in the first stage of pulmonary tuberculosis, less so in the second stage. It is not due to a specific influence upon the cause of the disease, but to an improvement in the condition of the blood,

in the appetite and in the general vigour. The authors consider the internal and the subcutaneous administration of the drug to be equally effective. They gave 0·2 to 0·3 grammes (3—5 grains) a day internally, and 0·05 to 0·1 grammes ( $\frac{3}{4}$ — $1\frac{1}{2}$  grains) a day subcutaneously.

In advanced cases of pulmonary tuberculosis, Bernheim, Gilbert and Fournier observed, apart from an improvement in the general health and in sleep, a remission of the cough, a decrease in the expectoration and the night sweats, especially when lecithin medication was combined with the use of guaiacol preparations. It should therefore always be given a trial in the second and third stages.

Bernheim and Rollo obtained particularly good results with the following prescription:

Rp. Lecithin.	1·0 grammie	
Guaiacol.	1·0 grammie	
Ol. oliv. spiritu lavati et sterilisati	10·0 grammes	
Sig. 1 to 2 c.c. to be injected subcutaneously on alternate days.		

Wilczinski prescribed lecithin for tuberculous women as an antimenorrhoeic with good results. (See under menstrual disturbances).

Kraus also considers lecithin a desirable aid in the nutrition of tuberculous patients. For, quite apart from any antibacterial and toxin-fixing properties, according to the author, it improves the patient's appetite without giving rise to secondary effects.

Dor reports a case of benign tuberculous meningitis. The patient was a woman aged 30, who had suffered for 3 months from haematemesis, wasting, cough, headache, optic neuritis and paralysis of the ocular nerves; the symptoms gradually grew worse, so that the development of tuberculous meningitis was apprehended. The author injected 1 grammie (15 grains) of lecithin subcutaneously on alternate days. For this purpose he used two preparations of lecithin, a solution of lecithin in oil, which had been prepared at 65° C., and a suspension of lecithin in oil prepared at the ordinary temperature. It was found that the solution prepared by heating caused a certain amount of discomfort, whereas the emulsion gave rise to a pleasant drowsiness. After only three injections the headaches had improved to such an extent that the

patient was able to go for short walks. On continuing the lecithin treatment, the improvement progressed, the turbid eye once more became bright, the skin became more highly coloured, there was an increase of 4 pounds in weight, and the ocular symptoms disappeared.

#### Form of Administration and Dosage of Lecithin.

It is apparent from the preceding communications that lecithin is used in the treatment of weakly children, in conditions of defective nutrition, in athrepsia, rickets, scrofula, anaemia and chlorosis; for adults in tuberculosis, debility following acute infective diseases, or following excesses, troubles of old age, conditions of exhaustion in consequence of mental overstrain, depression of mental and physical energy, pellagra, wasting, poverty of blood, secondary anaemias, metabolic diseases, diabetes, phosphaturia, osteomalacia, cerebro-spinal disease, nervous diseases, functional impotence, neurasthenia, general paralysis, tabes, psychoses, hysteria, migraine, nicotine amblyopia and menstrual troubles.

In most cases internal administration will suffice, and will be better tolerated by the patients on account of its simplicity and convenience, especially for prolonged administration. In order to make it as pleasant as possible for adults and children, and to mask the oily taste of pure lecithin, which many find disagreeable, I manufacture the following lecithin chocolate preparations, which possess a very pleasant taste:

Lecithin chocolate (Lecithin granulat.), a mixture of cocoa and sugar containing 10 p. c. of Lecithin Merck. It is specially suited for use in hospitals. One teaspoonful corresponds to 0.25 gramm (4 grains) of lecithin.

Lecithin chocolate tablets, made of chocolate, containing 0.25 gramm (4 grains) of Lecithin Merck. They may be prescribed for adults and children.

Lecithin cocoa tablets prepared from cocoa mass without sugar, containing 0.25 gramm (4 grains) of Lecithin Merck. They are intended for adults, who do not care for sweet chocolate, and may also be used in special cases, as for example in diabetes.

A normal dose for children is 0.25 grammie (4 grains) of lecithin twice a day, each dose corresponding to one lecithin chocolate tablet, or to one teaspoonful of lecithin chocolate; for adults 0.25 grammie (4 grains) of lecithin 3 to 4 times a day, e. g., 3 to 4 tablets or the same number of teaspoonfuls of lecithin chocolate.

Those wishing to use the older method of prescribing may take the following formulæ as models:

Rp. Lecithin Merck                            0.5 grammie ( $7\frac{1}{2}$  grains)  
Rad. Althææ pulv.  
Spirit. vini vel Glycerin.  
q. s. ut fiant pilul. No. 50.  
M. Sig.: 1 to 2 pills to be taken 3 times a day\*).

Rp. Lecithin Merck                            0.1 to 0.5 grammie ( $1\frac{1}{2}$ — $7\frac{1}{2}$  grains)  
Ol. Theobrom.                                2.0 to 3.0 grammes (30—45 grains)  
f. lege artis suppositor.

M. Sig.: One to be used daily.

Rp. Lecithin Merck                            2.0 grammes (30 grains)  
Ol. morrh.                                    500.0     "                    (17 oz)  
M. Sig.: 2 to 4 tablespoonfuls to be taken daily.

For subcutaneous (and intramuscular) injections, which are especially suitable in psychoses and weak digestion, Lecithin Emulsion Merck may be particularly recommended; it is a sterile emulsion of Lecithin Merck and water, containing 10 p. c. of lecithin, which I supply in ampoules containing 2 and 5 c. c. It is distinguished by its keeping properties. Children are given the contents of one ampoule of 2 c. c., corresponding to 0.2 grammie (3 grains) of lecithin, and adults the contents of a 5 c. c. ampoule, corresponding to 0.5 grammie ( $7\frac{1}{2}$  grains) of lecithin. The injections may be repeated daily or every 2 or 3 days, according to the nature of the case.

Before a satisfactory aqueous lecithin emulsion existed, lecithin was prescribed for subcutaneous use in an oily solution. There is no doubt that the emulsions are much preferable; but for general information and for special cases, mention may here be made of the older prescriptions:

\*) In administering small doses, lecithin tablets of 0.025 grammie ( $\frac{2}{5}$  grain) may be used.

Rp. Lecithin Merck	0·5 grammie
Ol. oliv. spiritu vini	
lavati et sterilisati	10 c. c.*)
M. Sig.: 1 to 3 c. c. to be injected on alternate days.	
Rp. Lecithin Merck	1·0 grammie
Guaiacoli pur.	1·0 grammie
Ol. oliv. spiritu vini	
lavati et sterilisati	10·0 grammes*)
M. Sig.: 1 to 2 c. c. to be injected on alternate days. (Tuberculosis.)	

### Lecithin in Veterinary Medicine.

As a result of ample experience, Fambach suggested lecithin for the treatment of inflammation of the brain and of cerebro-spinal fever (Meningitis subacuta and Meningitis cerebro spinalis) in horses, because it was the only drug known to be effective in the treatment of these diseases. But an essential condition is that lecithin treatment be begun at the earliest possible moment, i. e., in the first stage of the disease, as the result is otherwise doubtful. The medicament must be applied subcutaneously in suspension in normal saline solution, as oily solutions are absorbed too slowly. The ampoules supplied by me, containing 5 c. c. of lecithin emulsion, are best suited for this purpose, as Fambach mentions 0·5 grammie ( $7\frac{1}{2}$  grains) of lecithin as the normal dose for a horse. In slight cases the contents of one ampoule are injected daily, and in more severe cases two ampoules are used. The sterility of the lecithin emulsion is the best possible guarantee that the injections will cause no local symptoms of irritation; but the site of the injection should also be thoroughly cleansed and disinfected and the same preparation is absolutely essential for the injection syringes, as otherwise colonies of fungi will form in them. After injection, the site of the puncture is swabbed with a pledge of cotton wool soaked in absolute alcohol, and covered by ichthyol-collodion or iodoform-collodion. By adopting these precautions the injection is well borne. On repeating the injection, a different

\*) In dissolving lecithin, the temperature should not exceed 75° C. The sterile olive oil used for the solution should be previously purified by alcohol and then carefully freed from it, as otherwise a turbid solution is obtained which does not keep.

site should be chosen. In the cases treated by Fambach, the animals usually became more alert after 4 to 5 injections, and gradually returned to complete consciousness. The author recommends the continuation of the injections for several days after recovery has commenced. Fambach expects special benefit by his method of treatment in those cases in which the mental disturbances are caused entirely by transudations, which is the rule in the vast majority of horses. It is less promising in very severe cases, which are characterised by serous exudation or even cellular infiltration. H. Thum, although he considers lecithin a harmless preparation, did not find that the malady was made either better or worse by its employment. He therefore considers the dose suggested by Fambach to be too small.

Maintz draws attention to the value of lecithin in bone-formation and the promotion of bony growth, which in human medicine renders lecithin a favourite drug in rickets and osteomalacia; he recommends its trial for young horses, especially for valuable young breeders. Lecithin deserves special consideration in districts in which the soil only produces plants poor in lecithin, and the animals fed on these plants do not exhibit the desired perfect skeletal development. As the value of horses depends upon this to a great extent, the author expects good results from feeding young horses on small amounts of lecithin daily from the time of weaning until about the end of the second year.

With regard to the form of administering lecithin in veterinary practice, Holterbach suggests the following mixture for internal use:

Rp. Ovo-lecithin	5·0 grammes (75 grains)
Calc. phosph.	50·0     ,,     (1½ oz)
Magnes. carbon. q. s. ut f. pulv.	

This forms a dry, fine powder, which can easily be given to the animals. According to Holterbach, it keeps very well, but it is not advisable to store large quantities. Dogs are given a small teaspoonful in a little gruel 3 to 5 times a day.

#### Lecithin in Bacteriology.

Lecithin has not as yet attained any great significance in bacteriology.

In experimenting to obtain typhoid toxin, Bassenge made the discovery that lecithin emulsions have a most in-

jurious effect upon the growth of typhoid bacteria, and when sufficiently concentrated, may even cause the complete solution of the bacteria. The hope to which this discovery gave rise, that the resistive power of animals against typhoid might be raised by previous treatment by lecithin emulsions, has not been fulfilled. The author, however, succeeded in obtaining a typhoid toxin, which could be used for immunisation, by washing off typhoid cultures of 24 hours' growth with lecithin emulsion. This was used to treat guinea-pigs, which were infected 24 hours later with several times the lethal dose of typhoid bacteria, which they successfully withstood. This proves the bacteriolytic action of lecithin. It is still an open question whether it will be found of use in therapy.

Zeuner used lecithin for obtaining a tuberculosis toxin of high valency; he treated emulsions of lecithin and sodium oleate in water with virulent cultures of tubercle bacilli. Thus he obtained a toxin, which is said to be 5 times as strong as Koch's tuberculin. According to this, lecithin in combination with sodium oleate is capable of setting free large quantities of bacillary toxins.

Fromme worked out a method of facilitating the diagnosis and prognosis of puerperal fever. It is based upon the observations of Fromme and Gonnet that severe cases of puerperal infection are caused by a haemolytic streptococcus, while in mild cases and in healthy subjects non-haemolytic streptococci alone are present. Although their occurrence has not been recognised as a means of diagnosis, yet the fact remains that the majority of cases of severe illness are brought about by haemolytic streptococci. For the differentiation of this haemolytic streptococcus, Fromme recommended the so-called bouillon-lecithin test, and also another method which will not be described here. It is founded on the bactericidal property of lecithin, discovered by Bassenge. For further information, reference may be made to the communications of Fromme, Jacquin, Hamm, Mächtle, Sachs, Traugott and Thaler.

#### Tests for Purity of Lecithin.

Lecithin is prepared from animal and vegetable substances by extraction with organic liquids, such as ether, alcohol, methyl alcohol, etc. During this extraction, fats, cholesterin

and lecithalalbumins go into solution as well as the phosphatides, and they cause the impurity of the lecithin which remains after the solvent has been removed. The lecithins obtained from vegetable substances are especially rich in lecithalalbumins and are only freed from them with great difficulty. On the other hand, by means of a special process, pure lecithin can be obtained from yolk of egg. But in commerce so-called pure lecithins exist which contain a high percentage of cholesterin, fat and lecithalalbumin, making them unsuitable for therapeutic purposes. Special attention should therefore be paid to the chemical tests of this substance.

With the assistance of the data contained in the literature and of my own experience I have worked out an analytical test, with the help of which it is possible for every analyst to satisfy himself that the lecithin under examination meets the highest requirements. The practically 100 p. c. lecithin supplied by me is carefully examined in my laboratory by the method to be described, and can also be at any time controlled by others. I shall pay special attention to the further development of the method, because I am perfectly aware that only reliable analytical methods will be of value in distinguishing inferior commercial preparations, and in guarding the consumer from doubtful, so-called pure lecithins.

I. Lecithin should be a very hygroscopic mass of a yellowish-brown colour, which can be kneaded and which is not too soft and not transparent. (It should be noted that lecithin is a labile body, which on keeping must be protected from light, air and damp.)

II. Qualitative tests: An alcoholic solution of lecithin is precipitated by an alcoholic solution of cadmium chloride, with the formation of a yellow cadmium chloride compound\*).

A more reliable qualitative test is that of saponifying lecithin by means of baryta water and determining the products of decomposition which are formed. For this purpose a little lecithin is dissolved in ether, the solution is poured into

\*) As explained in detail by Thudichum, Erlandsen and Ulpiani the lecithins are capable of forming compounds with cadmium chloride. This fact is of no value for the quantitative estimation of lecithin, as the precipitation of lecithin by  $CdCl_2$  does not occur quantitatively. Compare also Heubner, Mac Lean, Strecker and Gilson.

baryta water, warmed on the water bath until the ether has evaporated, and then boiled for some time. The excess of barium hydroxide is removed by passing into the liquid carbonic acid and the precipitate is separated by filtration. The precipitate which remains on the filter contains the barium salts of the fatty acids; it is warmed with hydrochloric acid, left to cool and then shaken up with ether. The ether takes up the fatty acids. It has not as yet been possible to effect their separation, so that attempts to identify them would be useless. The filtrate, which contains the choline and the barium salt of glycerophosphoric acid, is evaporated to dryness and the residue extracted with alcohol. The choline goes into solution and, after conversion into the hydrochloride, can be identified by precipitation with gold chloride or platinum chloride. The barium glycerophosphate remains undissolved in alcohol; after ignition and solution in dilute nitric acid, it may be identified by the well known barium and phosphoric acid reactions.

III. Lecithin should form a clear solution in absolute alcohol and in ether. A solution of 1 gramm of lecithin in 10 grammes (12.5 c. c.) of alcohol should be perfectly clear.

IV. Lecithin should have only a faintly acid reaction, which appears admissible on account of the readiness with which lecithin is decomposed. If a drop of phenolphthalein solution (indicator) is added to 5 c. c. of the solution in alcohol (1:10) at most 4 drops of normal caustic potash will be required to produce a red coloration.

V. Phosphorus and nitrogen content: The most important criterion of the quality of lecithin is that it contains the correct amount of phosphorus and nitrogen. The estimation of phosphorus is important, as there are lecithins on the market the phosphorus content of which indicates that the amount of pure lecithin contained is very small. The estimation of nitrogen is essential, because lecithin, being a mono-amino-phosphatide, should contain phosphorus and nitrogen in a definite molecular ratio. Theoretically, the phosphorus content divided by the nitrogen content should give as result the figure 2.21. Practically, this figure is not usually reached, as the thorough purification of the mono-amino-phosphatide from other phosphatides is not practicable. But a pure commercial lecithin should certainly be required to give approximately the figure 2.

For the estimation of phosphorus, a useful method is that of direct weighing, recommended by Lorenz for small amounts of phosphorus (Landwirtschaftliche Versuchsstation 1901, Vol. 55, p. 183 and Lunge-Berl, Chemisch-technische Untersuchungsmethoden 1911, III., p. 23). In a silver crucible with a cover (or a platinum or porcelain crucible would do) about 1 gramme is weighed on the analytical balance; to this about 6 grammes of a mixture of 3 parts of anhydrous sodium carbonate and 1 part of sodium nitrate cryst.\* are added; the mixture is well kneaded with a nickel spatula, which is then wiped with a fragment of filter paper, which is also placed in the crucible. The cover is placed in position, and the crucible is first heated over a small flame and then over a larger flame until the mass becomes completely white. When the crucible has somewhat cooled, it is placed with the cover in a small glass beaker containing about 50 c. c. of water, which is warmed until the contents of the crucible are completely dissolved. This solution is poured into a measuring flask with a capacity of 200 c. c., the crucible and beaker are rinsed with water and the latter added to the contents in the flask which is then filled up to the mark with water. 20 c. c. of this solution are transferred to a beaker, neutralised with nitric acid (sp. gr. 1.3), and made up to 30 c. c. with water. To this solution 20 c. c. of nitric acid containing sulphuric acid (see under reagents on page 48) are added, and the whole is heated over wire gauze until the first bubbles arise; then the flame is removed, the beaker is gently shaken for a few seconds, and 50 c. c. of molybdenum sulphate reagent are poured into the middle of the mixture. The mixture is then left to stand for 2 to 5 hours, after which it is filtered through a Gooch crucible containing asbestos, which has been dried at 100° C. and allowed to cool in the air. It is then washed out 4 times with a 2 p. c. ammonium nitrate solution, the crucible is filled completely once and twice half full with absolute alcohol, the washing out is repeated in the same way with anhydrous ether. It is then drawn off, and the crucible with its contents are dried in a vacuum exsiccator for 30 minutes without sulphuric acid and without calcium chloride. It is then immediately weighed.

\* ) Compare W. Fresenius and Grünhut, Zeitschrift für analytische Chemie 1912, p. 102.

The calculation is founded on the assumption accepted by the majority of authors that lecithin is a mixture of triolein-lecithin, tristearin-lecithin and tripalmitin-lecithin. A lecithin of this nature would theoretically contain 3.94 p. c. of phosphorus. This assumption is known not to correspond exactly with the facts, and therefore this percentage of phosphorus is never quite reached. It is, however, justifiable to demand that lecithin should contain 3.5 to 3.7 p. c. of phosphorus, i. e., 90 to 94 p. c. of the theoretical content based on the above assumption.

Calculation: If  $x$  grammes of precipitate have been weighed, the percentage of  $P_2O_5$  contained will be:

$$\frac{x \cdot 0.03295 \cdot 100}{\text{substance used}}$$

the percentage of phosphorus will be:

$$\frac{x \cdot 0.014398 \cdot 100}{\text{substance used}}$$

If the percentage of phosphorus is multiplied by 25.39, this will give the percentage of lecithin in the preparation under examination.

The following reagents are required for the examination described:

1. Molybdenum sulphate reagent: 100 grammes of pure, dry ammonium sulphate are dissolved in 900 c. c. of nitric acid (sp. gr. 1.4) and 100 c. c. of water in a two litre flask. 300 grammes of ammonium molybdate are dissolved in hot water in a litre flask, which, when cool, is filled up to a litre with water. This solution is poured in a thin stream into the ammonium sulphate solution, and the mixture is left to stand for 48 hours; it is then filtered through an acid-fast filter and kept in the dark.
2. Nitric acid containing sulphuric acid: 30 c. c. of sulphuric acid (sp. gr. 1.84) are added to a litre of nitric acid (sp. gr. 1.2) and the whole mixed.
3. 2 p. c. aqueous ammonium nitrate solution: Unless already faintly acid, a few drops of nitric acid are added per litre.

The estimation of nitrogen is carried out by Wilfarth's method (Chemisches Zentralblatt 1885, p. 17 and 113). About 1 grammé of lecithin is placed in a Kjeldahl flask, and about 30 c. c. of concentrated sulphuric acid containing 9 p. c. of phosphoric anhydride are poured on to it and then 0·7 grammé of yellow mercuric oxide is added. This is heated until the mixture becomes colourless, allowed to cool, diluted and washed into a large Erlenmeyer flask. Next, nitrogen-free solution of caustic soda (sp.gr. 1·3) is added until the mixture becomes alkaline, and then 10 c. c. of potassium sulphide solution (1:10). It is distilled into a receiver containing 25 c. c. of  $\frac{1}{5}$  normal hydrochloric acid. 1 c. c. corresponds to 0·0028 grammé of nitrogen.

A lecithin which, as was assumed above, consists of equal parts of dioleyl-lecithin, dipalmityl-lecithin and distearyl-lecithin, should theoretically yield 1·77 p. c. of nitrogen. Pure commercial lecithin yields 1·9 to 2 p. c. (With regard to the estimation of lecithin in tablets, lecithalbumins, etc., compare Virchow; with regard to the estimation of lecithin in oils, compare W. Fresenius and Grünhut.)

A further criterion of the purity of lecithin is its iodine value. This also gives information as to how far the auto-oxidation of the preparation has advanced and will therefore only be of value in lecithin which has been properly kept, and which is not too old. In my experience, a good commercial lecithin has an iodine value 60 to 65. For its determination, about 0·5 grammé of lecithin is dissolved in 10 c. c. of chloroform in an Erlenmeyer flask with a glass stopper. To this solution are added 30 c. c. of iodine-mercury chloride solution which has been prepared 48 hours previously according to the formula given in the German pharmacopœia, and it is allowed to stand overnight. Then a solution of 1·5 grammes of potassium iodide in 15 c. c. of water is added, the mixture is diluted with 100 c. c. of water, and if necessary, more potassium iodide solution is added until the precipitate re-dissolves; it is then titrated with  $\frac{1}{10}$  normal sodium thiosulphate solution. A control experiment is carried out simultaneously. If a represents the experiment with lecithin and b the control experiment, then

$$\frac{(b-a) \cdot 1\cdot2692}{\text{substance used}} = \text{Iodine value.}$$

VII. A lecithin emulsion prepared with water should be white in colour. 0·5 gramme of lecithin is dissolved in 10 c. c. of ether and this solution is added gradually, shaking well, to 10 c. c. of water. Into this mixture a current of hydrogen is slowly passed, the mixture being at the same warmed by placing it in warm water until it no longer smells of ether. The emulsion obtained should at the most be slightly yellow.

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## Preparations and Drugs.

### Abrin.

Among the newer remedies for cancer, the active principle of the seeds of *Abrus precatorius* (*Jequirity*) deserves mention. Its therapeutic efficacy has been studied for a number of years by R. Rampoldi. According to him, abrin has a destructive action upon epithelioma, but also promotes the growth of new epithelium. A number of authors\*) verified Rampoldi's statements, obtaining very satisfactory results. Rampoldi has so far dealt with 110 cases; by the employment of his method they were cured and the cosmetic results were most satisfactory. The method of treatment consists in the external application of an extract of jequirity in the form of ointments or of gelatin discs. Thus, its indication is limited to cutaneous cancer and to accessible cancer of the mucous membranes. The results obtained in cutaneous cancer especially render the prospect of further trials most hopeful. The length of treatment varies enormously, for while some cases may be cured in a few weeks, others may take many months.

A special preparation, which may be of service for Rampoldi's treatment, is the "Jequiritin of Rampoldi and Capini", which figures in the Italian pharmacopœia. According to this, liquid jequiritin is a fluid extract of jequirity seeds and is prepared in 5 different strengths. No. 1 has a strength of 4 p. c., No. 2 of 8 p. c., No. 3 of 12 p. c., No. 4 of 16 p. c., and No. 5 of 20 p. c. The gelatin discs are prepared from the jequirity fluid extract in such a way that one small

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Rampoldi, Giornale Italiano delle malattie veneree e della pelle 1912, Vol. 52, F. 6, p. 755. Compare also Annali di Ottalmologia 1907—1909.

\*) Fumagalli, Bialetti, Farina, Denti, Annali di Ottalmologia 1909, Vol. 39. — Nobile, Grignolo, ibid. 1910, Vol. 39. — Litala, Boggi, Baquis, ibid. 1911, Vol. 40. — Seganti, La Stomatologia Vol. 7, No. 12. — Parascandolo, ibid. Vol. 9, No. 3. — Comotti, ibid. Vol. 9, No. 11. — Pollini, Lo Specialista moderno 1910, Dec. — Merlo, Nasimbeni, ibid. 1911. — Traina, Atti della Riunione della Società Italiana di Patologia 1908. — Maccabruni, Giornale Italiano delle malattie veneree e della pelle 1912, 716. — Nobile, ibid. — Farina, ibid. p. 762. — Dori, ibid. p. 763. — Cattaneo, ibid. p. 766. — Rossini, ibid. p. 768.

disc corresponds to 0.0045—0.006—0.009 grammes of fluid extract. Jequiritin ointment contains 10 p. c. of fluid extract.

These preparations were originally only intended for the ophthalmic treatment of chronic inflammation of the eyes\*).

### Acetonitrile.

The reaction of Hunt, or Ghedini, depends, as is known\*\*), upon the increased resistance of mice against acetonitrile, after being fed upon thyroid substance. The value of this reaction has recently been questioned by H. O. Lussky on the ground of his pharmacological experiments. The author found that the resistive power of mice against acetonitrile is not diminished by extirpation of the thyroid gland and remains as great as that of normal animals. He further demonstrated that the resistive power of mice, fed on the blood of dogs and rabbits which had for some time received thyroid gland substance, was not increased. It was, on the other hand, increased in mice fed on the blood of thyroidectomized rabbits. Thus, Ghedini's reaction is apparently not specific.

### Acetyl-Salicylic Acid.

In comparing the therapeutic action of acetyl-salicylic acid and sodium salicylate in rheumatism, Roch came to the conclusion that acetyl-salicylic acid could not be regarded simply as a substitute for sodium salicylate, as it exerted a very special action on the fever and on subacute rheumatism. Its antipyretic power is much more marked than that of sodium salicylate, as is apparent especially in the fever of phthisical patients. In these cases, while the action of even 2 to 3 grammes (30—45 grains) of sodium salicylate was uncertain, the author was able to bring about an immediate decrease of temperature lasting 2 to 3 hours by giving only 0.5 to 1 gramme ( $7\frac{1}{2}$ —15 grains) of acetyl-salicylic acid; the action resembled that obtained by the administration of 2 grammes (30 grains) of antipyrine, or of 1 gramme (15 grains) of pyramidon. Roch also attributes to acetyl-salicylic acid

\*) Compare Jequiritol in Merck's Report 1909, p. 47.

\*\*) Merck's Report 1911, p. 132.

Lussky, American Journal of Physiology 1912, Vol. 30, p. 63.

Roch, Hirtz, Bardet, Münchener medizinische Wochenschrift 1912, No. 16, p. 902.

a greater analgesic effect than is possessed by sodium salicylate. Hirtz is of a different opinion. For articular rheumatism he considers sodium salicylate far superior to acetyl-salicylic acid and believes the latter to be an uncertain antipyretic. With regard to the preference extended to sodium salicylate on account of its ready solubility rendering it suitable for rectal administration, the argument is less sound, because in place of acetyl-salicylic acid its readily soluble salts may be employed. Free salicylic acid is also dissolved with difficulty. On the other hand, the use of aromatic salicylates, such as aspirin, apparently gives rise to greater danger of cutaneous irritation than arises from the use of salicylic acid; this secondary effect, according to Bardet and Dallaz, must be attributed to the aromatic residue rather than to the salicylic acid residue. As the secondary effects of aspirin are usually due to idiosyncrasy of the patient, Dallaz suggests beginning with doses of 0·25 gramm (4 grains) of aspirin and only increasing the dose to 0·5 gramm ( $7\frac{1}{2}$  grains) after having ascertained that the patient tolerates the drug well.

C. Lewin has made several communications on the calcium salt of acetyl-salicylic acid—Kalmopyrin. According to these, it has proved a useful salicylic preparation for rheumatism, lumbago, coryza, influenza and also for the pain accompanying tabes and carcinoma. The author considers the chief value of the drug to be its ready solubility, which renders it especially suitable for children. The calcium component may be an additional advantage, especially in the treatment of coryza and of all affections accompanied by exudations.

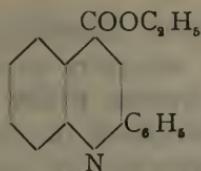
### Acitrin.

The ethyl ester of 2-phenyl-cinchoninic acid\*) is placed on the market under the name of acitrin. Acitrin is a pale yellow, crystalline powder, without smell or taste, melting at  $60^{\circ}$ — $61^{\circ}$  C. It dissolves with difficulty in water, more readily in alcohol, ether, chloroform and benzol. Its chemical formula is:

Dallaz, Presse médicale 1912, No. 28, p. 288.

Lewin, Therapie der Gegenwart 1912, No. 11, p. 509.

\*) Compare Merck's Report 1911, p. 135 and Apotheker-Zeitung 1912, p. 818.



The pharmacological action of acitrin is that of free phenyl-cinchoninic acid, but the excretion of uric acid does not commence as early as is the case with the free acid. Therefore the excretion of urates is said to be rare, and thus colic due to renal calculi, such as has been observed after administration of phenyl-cinchoninic acid, can be avoided. The total excretion of uric acid is the same as when the free acid is used. Like it, acitrin is indicated in uratic deposits, especially in gout and in articular rheumatism. A dose of 0·5 to 1 gramm (7½ to 15 grains) in water is administered 3 to 4 times a day, preferably an hour after meals.

### Actinium.

A. E. Stein has studied\*) actinium and its therapeutic value. For his experiments he used compresses soaked with a substance containing actinium (so-called radiofirm compresses), which were fixed in a convenient way to the part of the body requiring treatment. The chief indications for these compresses are found in rheumatic, gouty and neuralgic affections, but the author also obtained satisfactory results in several other forms of disease, particularly in nervous headache, buzzing in the ears and other nervous disturbances. He also saw good results in several cases of chronic bronchial affections. However, the employment of actinium compresses must on the whole be considered as supplementary to other measures, especially those of a physical nature. The author considers actinium treatment to be of special value in combination with diathermic treatment.

P. Lazarus reports upon the employment and action of actinium in pernicious anaemia. He injected the preparation

Stein, Berliner klinische Wochenschrift 1912, No. 17, p. 784. — (Münchener medizinische Wochenschrift 1911, No. 24, p. 1302.)

\*) Compare Merck's Report 1911.

Lazarus, Allgemeine medizinische Zentral-Zeitung 1912, No. 46, p. 607. — Deutsche medizinische Wochenschrift 1912, No. 46, p. 2193.

intramuscularly and also administered it in the form of draughts. In a case refractory to arsenic, he thus obtained improvement of the general health, of the condition of the blood, of the appetite and of the body-weight. The number of erythrocytes rose after the first course of actinium treatment from 1.3 to 2.6 millions, and after the second course to 6.5 millions.

### Adalin.

Further communications on the action of adalin\*) have been made in the past year by J. von Ehrenwall, E. Glombitzka, H. Gudden, B. Haake, E. Impens, Mohr, Skutetzky, R. Traugott, X. Walter, M. Weissbart, W. Gemski, K. Tiling, Tauszk and F. Lube.

Impens demonstrated experimentally that adalin is split up in the animal organism and is excreted in the urine, partly in the form of an inorganic and partly in organic combination (possibly  $\alpha$ -bromo-diethyl-acetic acid and unaltered bromo-diethyl-acetyl urea). E. Filipi, on the other hand, in his pharmacological examination of adalin in the urine, found no inorganic bromine. He also repeatedly points out that adalin produces its hypnotic action as such, while the decomposition products only play a subsidiary part. He therefore deprecates the suggestion of Hoppe and Seeger, to administer adalin rectally dissolved in caustic soda, because adalin, when

\*) Compare Merck's Report 1910 and 1911.

Ehrenwall, Therapeutische Monatshefte 1912, No. 4, p. 253.

Glombitzka, Münchener medizinische Wochenschrift 1912, No. 6, p. 307.

Gudden, Münchener medizinische Wochenschrift 1912, No. 2, p. 83.

Haake, Allgemeine medizinische Zentral-Zeitung 1912, No. 3, p. 29.

Impens, Therapie der Gegenwart 1912, No. 4, p. 158.

Mohr, Journal médical de Bruxelles 1912, Vol. 17, 6<sup>th</sup> June.

Skutetzky, Prager medizinische Wochenschrift 1912, No. 11.

Traugott, Berliner klinische Wochenschrift 1912, No. 3, p. 115.

Walter, Wiener klinische Wochenschrift 1912, No. 26, p. 1006.

Przeglad lekarski 1912, p. 175.

Weissbart, Heilkunde 1911, No. 24.

Gemski, Srowski Tygodnik lekarski 1912, p. 5.

Tiling, Therapeutische Monatshefte 1912, No. 10, p. 711.

Tauszk, Allgemeine Wiener medizinische Zeitung 1912, No. 31.

Lube, Dissertation, Göttingen 1912.

dissolved in the alkali is split up and probably only a part of it displays its action.

Gemski employed adalin as a hypnotic and sedative with satisfactory results in a fairly large number of cases. In his experience doses of 0·5 to 1 gramme ( $7\frac{1}{2}$  to 15 grains), after 30 to 60 minutes, produce sleep lasting 6 to 8 hours, in which respiration is somewhat slowed, the pulse rate and blood pressure are slightly lowered. He never observed injurious secondary effects. In febrile diseases, such as pneumonia, typhoid and erysipelas, on the other hand, the hypnotic effect is said to be very slight. Skutetzky, Mohr and Walter are of the same opinion. Walter especially emphasises the favourable hypnotic and sedative action of the drug in cardiac neuroses and in diseases of the heart and vessels. Mohr also considers adalin to be harmless in cardiac affections. He suggests doses of 0·75 to 1·5 grammes (12—24 grains), to be administered in warm sugar and water.

Adalin, according to Gudden and Haak, is useful in nervous diseases, e. g., in the numerous cases of insomnia consequent upon neurasthenia, hysteria, angina pectoris, dementia praecox, etc. Gudden is in favour of giving a sufficiently large dose, of 1 to 1·5 grammes (15 to 24 grains), because thus the duration of the stage of excitement, which usually precedes the commencement of sleep if too small a dose be given, is rendered shorter. A further indication for adalin is furnished, according to Haake, by cases of bronchial asthma occurring in young, nervous individuals. In most cases, by administering 0·5 gramme ( $7\frac{1}{2}$  grains) 3 times a day, he succeeded in cutting short a commencing attack, or rendering it less severe. In nervous asthma the hypnotic action of adalin also proved satisfactory. Tiling gave doses of 0·5 to 1 gramme ( $7\frac{1}{2}$  to 15 grains) of adalin in bronchial asthma and emphysema which was not too far advanced, and found that the breathing became quieter and the provocation to cough was lessened. The author also emphasizes its successful employment in chronic myocarditis and in valvular affections with loss of compensation, in which repeated doses of 0·5 gramme ( $7\frac{1}{2}$  grains) brought about tranquillisation of mind and subjective improvement.

Haake prescribed adalin for children in cases of convulsions due to rickets or anaemia. He gave 0·25 gramme

(4 grains) 3 times a day, and found that it caused the cessation of the attacks within a short time.

v. Ehrenwall, who used adalin with benefit in nervous disturbances and mental diseases, seeks its indication in the diseases of children, old people, alcoholics, pregnant women, and also in psychoses which are accompanied by organic disease, especially by cardiac disease, and by pregnancy. Cases of failure principally occur where the physical pain is too great, or where there is exaggerated excitability. The author administered doses ranging from 0·25 to 2 grammes (4 to 30 grains). If after an hour the desired effect had not ensued, he gave another dose of 1 to 1·5 grammes (15 to 24 grains), and in severe cases he even prescribed this dose 3 times in the course of a night.

Globitz summarises his results in mental cases as follows: Adalin is of marked benefit as a sedative in all cases of slight and fairly severe hallucinatory and motor excitement, and especially in those belonging to the dementia praecox group, in senile dementia, hysteria, mania and also in conditions of fear with depression and in imbecility. But in cases of severe excitability, especially in those which originate in hallucinations, even large doses are useless. Its advantages are: almost complete tastelessness, rapid excretion and the fact that no habit is acquired. Its disadvantages: a certain irregularity of action on the prolonged administration of large doses, the possibility of the appearance of toxic symptoms, especially if it is combined with other medicaments, and the very high price, both absolute and relative, on account of the large doses required in order to obtain a satisfactory result.

### Adamon.

This new drug\*) was employed with benefit by F. Bogner in 40 cases of slight excitability, nervous tachycardia and nervous palpitation. The preparation has only a sedative and no hypnotic action. In palpitation, the subjective troubles were soon diminished, the rapidity of the pulse was favourably affected, but the blood pressure was not noticeably reduced. The remedy was well borne by

\*) Compare Merck's Report 1911, p. 211.

Bogner, Medizinische Klinik 1912, No. 2, p. 64.

the stomach and intestine and gave rise to no troublesome secondary effects. Doses of 0·5 grammie ( $7\frac{1}{2}$  grains) were administered 3 to 5 times a day.

v. Rad extended the field of application of adamon. He tried it not only in mild conditions of excitement, e. g., in neurasthenia, hysteria and alcoholism, but also in milder forms of depression of cyclical mania, in persons suffering from delusions, in troubles of the climacteric and in cardiac neuroses. The sedative action was in most cases highly satisfactory and occasionally the patients became so calm that the administration of hypnotics was superfluous. An action of this kind can, of course, only be expected in suitable, quite mild cases, in which the suggestive effect also plays an important part. Adamon therapy, according to von Rad, is also suitable for cases of agoraphobia and claustrophobia, as adamon tablets need not be dissolved in water. They can readily be chewed up and swallowed, so that the patients can carry them in their pockets and take them at any time. The author does not say whether the action is partially suggestive in these cases also. The single doses varied between 0·5 and 2 grammes ( $7\frac{1}{2}$  to 30 grains) and he gave up to 3 grammes (45 grains). He considers the frequent administration of small doses to answer the purpose better than a single large dose. On the average, he found 2 to 4 tablets (of 0·5 grammie [ $7\frac{1}{2}$  grains] each) a day to be sufficient. Stulz came to similar conclusions.

According to R. W. Frank's communications, adamon appears to be an excellent remedy for irritative symptoms of the urogenital system. The author gave an average dose of 3 grammes (45 grains) of the preparation, one-third of which was taken at half-hourly intervals during the last hour and a half before going to sleep. In the well known troubles of the acute stage of gonorrhœal infections, painful erections interfering with sleep and frequent emissions, it has proved a promptly acting medicament. In one case only it had no evident effect, which the author is unable to explain. Only one observation has been made on the effect of adamon on pathologically increased sexual desire, which, however, gives promise of good results.

Rad, Therapie der Gegenwart 1912, No. 2, p. 93.

Stulz, Therapie der Gegenwart 1912, No. 12, p. 576.

Frank, Deutsche medizinische Wochenschrift 1912, No. 49, p. 2309.

**Afridol.**

As afridol (the sodium salt of oxy-mercury-o-toluic acid\*), contains a high percentage of mercury, L. Meyer tried it in syphilis. He used a 2 p. c. solution and injected 2 to 8 c.c. of it intravenously, but the result was not satisfactory. The author considers this to be due to the fact that even large doses of mercury, which rapidly leave the organism, can exercise no lasting influence upon the virus of syphilis.

Afridol was used by R. Müller and F. Schmid in the form of a soap in various skin diseases. According to Müller, the action of the preparation was so excellent in ringworm of the scalp of children and in parasitic sycosis, and also in the trichophytosis known as ringworm of the hairless regions of the body, that in the first named diseases a cure was frequently effected without epilation. Afridol soap is also specially efficacious in the different forms of acne. In these cases the comedones and acne pustules usually heal in the course of 1 to 2 weeks by simply washing the affected part and allowing the soap lather to dry over night, without the administration of medicaments and without the employment of pastes causing desquamation. In furunculosis, the inflammatory infiltrations not only disappear with comparative rapidity by treatment with afridol, but the appearance of new furuncles is prevented. In impetiginous eczema (pediculosis), afridol soap is of use in place of white precipitate ointment, and also in seborrhœa. In psoriasis, on the other hand, lasting results were not obtained, even though there was a marked temporary improvement. Schmid confirms the beneficial properties of afridol soap. He and Görl are of opinion that, if used as a shaving soap, it constitutes a good prophylactic and curative for ringworm.

E. Neumark also considers afridol soap useful as a disinfectant for the skin and for surgical instruments.

\*) Compare Merck's Report 1910.

Meyer, Dermatologische Zeitschrift 1912, No. 4.

Müller, Deutsche medizinische Wochenschrift 1912, No. 12, p. 563.

Schmid, Therapie der Gegenwart 1912, No. 6, p. 271.

Görl, Münchener medizinische Wochenschrift 1912, No. 3, p. 169.

Neumark, Hygienische Rundschau 1912, p. 1353.

**Agar-Agar.**

C. Schindler recommends an aqueous jelly, consisting of 0.5 p. c. of sterile agar, as a vehicle for antigenorrhœic remedies. It is prepared from the 2.5 p. c. water-agar, made by me according to a special formula, which in suitable dilution remains sufficiently fluid at the ordinary temperature to be drawn up into a gonorrhœa syringe. It should be specially noted that a preparation of this description cannot be obtained by the solution of any kind of agar. The agar sterilisat. 2.5 p. c. supplied by me, after dilution with sterile water, is added to the antigenorrhœic to be used. The author suggests the following formula:

Rp. Agar steril. (Merck) 2.5 p.c.	40.0 grammes
Massæ leni calore liquefactæ	
adde	
Aq. destill.	160.0 ,,
post refrigerationem conserpe	
recenter	
Protargol	1.0 gramme
(sive Albargin, Ichthargan, etc.)	

According to Schindler, agar jelly is a suitable constituent for antiseptics in general, and by the addition of dextrin or gum acacia, protargol and silver pencils can be prepared. The more intensive action of the antigenorrhœic drug, when applied in the jelly, is certainly due to the dilatation of the urethra, and to a part of the jelly remaining on the mucous membrane after the main mass has been extended. The injection of protargol-agar jelly can be recommended along with vaccine treatment, especially in vaginal gonorrhœa of children. As much as possible is injected by means of the gonorrhœa syringe, so that the vaginal folds are opened up, and the vagina is closed by means of a plug of cotton wool, suitably enclosed in guttapercha tissue.

For intestinal treatment M. Einhorn gives a formula for combining drugs with agar, in which the agar serves partly as a vehicle, and partly, as in the case of regulin, to swell the intestinal contents. The medicament in question

Schindler, Münchener medizinische Wochenschrift 1912, No. 18.

Einhorn, Berliner klinische Wochenschrift 1912, No. 3, p. 114.

American Journal of Medical Sciences 1912, p. 230. Pharmazeutische Zeitung 1912, p. 177.

is dissolved in boiling, aqueous agar solution, and then evaporated down to the original volume of dry agar; the preparation thus obtained is coarsely ground. By this method the author has prepared (30 p. c.) phenolphthalein-agar, and also compounds of agar with rhubarb, calumba, gambir, tannin, simaruba, myrtillus, ipecacuanha and sumbul, and has used some of them with benefit in the presence of suitable indications.

For the qualitative and quantitative analysis of amylopsin, steapsin and trypsin in the pancreatic juice, M. Einhorn has elaborated a method, for which so-called agar tubes are required. Three varieties of tubes are prepared according to the following formulas:

1. Starch tubes. 5 grammes of starch and 2.5 grammes of agar powder are ground to a thin paste with a little water, 2 grammes of tincture of iodine U.S.P.\* and enough water are added to bring the total weight of the mixture up to 100 grammes. The mixture is heated to boiling and introduced into capillary glass tubes having an internal diameter of 1 to 1.5 mm. These are cut into lengths of 3 cm., and when cool, their ends are sealed up with paraffin.

2. Olive oil tubes. 1 gramme of olive oil and 2.5 grammes of agar powder are ground to a thin paste with a little water, 1 gramme of phenolphthalein solution U.S.P.\*\*) and 0.5 gramme of aqueous 5 p. c. caustic potash solution are added and the mixture is made up to 100 grammes with water. The further procedure is as described under 1.

3. Hæmoglobin tubes. 1 gramme of hæmoglobin and 10 grammes of water are mixed to form a homogeneous mass, 2.5 grammes of agar powder are added and the mixture made up to 100 grammes with water. The further procedure is the same as described under 1.

If these little tubes, after removal of the paraffin plug, are treated in a suitable way with the contents of the duodenum for 16 to 22 hours at the temperature of the blood, the dark blue colour of the starch tube, the red colour of the olive oil tube and the brown colour of the hæmoglobin tube will disappear for a greater or less distance from the opening

Einhorn, Berliner klinische Wochenschrift 1912, No. 44, p. 2079.

\*) 7 grammes of iodine, 5 grammes of potassium iodide and alcohol 95 vol. ad 100 c. c.

\*\*) 1 gramme of phenolphthalein, 50 c. c. of alcohol and 50 c. c. of water.

of the tube, according to the amount of ferment present. This reaction only takes place in the presence of the specific ferments, and not if the pancreatic juice is first boiled and the ferments thus destroyed.

### Airol.

Airol was recommended years ago by Bernheimer for the treatment of ophthalmic-blennorrhœa, and he described in detail the method of employing the drug. Recently the advantages of this method have been confirmed by F. von Herrenschwand, who also pointed out that airol treatment was superior to that by preparations of silver. In contrast with the latter, airol, in the presence of albumin and sodium chloride, is said to be more injurious to gonococci and to stimulate phagocytosis better. As Bernheimer had already assumed, the action depends upon the bactericidal properties and the property of inhibiting bacterial growth of the iodine which is liberated from the airol (bismuth-oxy-iodo-gallate), upon the astringent action of the gallic acid as well as the drying properties of the bismuth. Further trials in ophthalmic-blennorrhœa neonatorum and adulorum therefore appear justifiable\*).

### Alcohol.

In a paper on the disinfecting power of alcohol, A. Beyer shows that 70 p. c. alcohol is the best disinfectant, while both higher and lower percentages of alcohol are apparently less suitable for this purpose. This discovery is of practical importance, seeing that alcohol is widely employed as a disinfectant for the skin. The maximum efficacy of 70 p. c. alcohol is due to the fact that alcohol with increasing concentration penetrates less and less into albumin, while coagulating it more and more. According to Beyer, absolute alcohol, in the absence of moisture, even has a preservative action on bacteria. With the highest possible percentage of

Bernheimer, Klinische Monatsblätter für Augenheilkunde 1906,  
No. 2 and 3.

Herrenschwand, Archiv für Ophthalmologie 1912, Vol. 82, p. 372.

\*) Compare Merck's Report 1906, p. 25.

Beyer, Zeitschrift für Hygiene 1912, Vol. 70, No. 2. — Zentralblatt für die gesamte Therapie 1912, No. 8, p. 447. — Berliner klinische Wochenschrift 1912, No. 26, p. 1254.

alcohol on the one hand, and a sufficient amount of water on the other, the optimum action is attained. Concentrations over 70 p. c. are less efficacious on account of the insufficient amount of water. The author further points out that a mixture of alcohol and ether, or chloroform, benzol, glycerin or acetone is not more efficacious than 70 p. c. alcohol. E. Frey also believes 70 p. c. alcohol to have the best bactericidal action.

Schumburg considers absolute alcohol to be an excellent disinfectant for the hands and the skin. Three to five minutes suffice for disinfection. Alcohol also saves the skin better than other preparations, if it has not been previously softened by soaps. By previously washing with water, the alcohol may be diluted and thus partially deprived of its efficacy. Following the recognition of the excellent bactericidal properties of alcohol, the author expects that it will be extensively used in surgery, dermatology and medicine.

Marquis also deprecates the previous washing with soap in the disinfection of the hands. In his opinion, the power of alcohol as a disinfectant varies directly with its strength. With regard to the concentration of alcohol in bacteriological experiments, he does not consider it possible to demonstrate which concentration between 60 and 100 p. c. has the most pronounced bactericidal action. In practice, he considers it essential that the hands should not be merely dipped into alcohol and rubbed against one another, but that they should be rubbed with alcohol for 10 minutes by means of cotton wool swabs. The disadvantage of this method is that the blood adheres to the hands, its advantage lies the speed and simplicity with which it may be carried out.

V. Horsley has discussed the value of the internal administration of alcohol. He considers the drug both useless and harmful in pneumonia, shock, etc., whereas other authors have found it useful in suitable doses, e. g., Cushing as an anodyne in unbearable pain; Smith, Lauder Brunton,

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Frey, Deutsche medizinische Wochenschrift 1912, No. 35, p. 1633.  
Schumburg, Deutsche medizinische Wochenschrift 1912, No. 9, p. 403.

Marquis, Revue de chirurgie 1912, No. 2.

Horsley etc., Klinisch-therapeutische Wochenschrift 1912, No. 32, p. 951. — Münchener medizinische Wochenschrift 1912, No. 31, p. 1741. — See also Brit. Med. Journal 1912, I, page 894 and 1074.

Stoddart and Brown as a stimulant to digestion and appetite; Corner in chronic rheumatism and respiratory troubles of old people; Goodall for colic and diarrhoea occurring in the course of measles; Currie for cardiac debility following diphtheria, and so forth.

The value of alcohol injections in trigeminal neuralgia is reported upon by H. T. Patrick, K. Otto, Struycken, J. Dollinger, W. Harris, W. Alexander, Sicard and Leblanc, Mainzer, Haertel and A. Gordon. According to these authors, injections of alcohol form a means of cutting short severe trigeminal neuralgia, or of getting rid of it for a prolonged period. Harris observed recurrences after 2 months to 2½ years, Patrick after six months to 4 years. According to Dollinger, relapses occur after 1 to 5 months, but they are not of the same intensity as the original attacks, and they are cured by repeating the injections. It cannot yet be decided whether a definite cure is possible in isolated cases. All authors are agreed that if internal treatment proves unsuccessful, alcohol injections should always be tried before resorting to the resection of the Gasserian ganglion. The injections, being free from danger, can be carried out by any medical man, while for the operation a very experienced surgeon is required. Patrick suggests that young, vigorous people should undergo the operation, and old and weak individuals should be treated by injections. Dollinger and Harris enlarge upon the technique and dosage. Reference must be made to the original work for details, as they cannot well be briefly summarised. According to Mainzer,

Patrick, Journal of the American Medical Association 1912, January 20. — Wiener klinische Wochenschrift 1912, No. 11, p. 426.  
Otto, Mitteilungen aus den Grenzgebieten der Medizin und Chirurgie 1912, Vol. 25, No. 1.  
Struycken, Monatsschrift für Ohrenheilkunde und Laryngo-Rhinologie 1912, p. 661.  
Dollinger, Deutsche medizinische Wochenschrift 1912, No. 7, p. 297.  
Harris, Lancet 1912, No. 4613, p. 218.  
Alexander, Deutsche medizinische Wochenschrift 1912, No. 6, p. 271.  
Sicard-Leblanc, Presse médicale 1912, No. 54, p. 573.  
Mainzer, Münchener medizinische Wochenschrift 1912, No. 30, p. 1689.  
Haertel, Münchener medizinische Wochenschrift 1912, No. 49, p. 2705.  
Gordon, Journal of the American Medical Association 1912, January, 13.

the prognosis in cases which have undergone operation is unfavourable for treatment with alcohol injections.

E. Paul-Boncour recommends the injection of 1 c.c. of alcohol (90 p. c.) into the superior laryngeal nerve for the treatment of dysphagia in laryngeal tuberculosis. Deglutition and the ability to take nourishment are rendered easier for about 3 weeks, after which period the injection may be repeated. The author has also observed the inhibition of tuberculous processes as a result of this method of treatment. The technique of these injections can be learned from the references noted below.

### Alcohol, Methyl

In the past year a large number of observers have studied the question of poisoning by methyl alcohol, its various symptoms, its cause, its transient and permanent injuriousness, its fatal termination, and the dangers of methyl alcohol in general. These include, among others, Lewin, Rost, Levy, Strassmann, Foerster, Schenk, Ohlemann, Mendel, Hirschberg, Harnack, Grunow, Völtz, Keferstein, Kühn, Bürger, Pick, Schmiedeberg, Buckha,

Paul-Boncour, *Progrès médical* 1912, No. 20. — *Deutsche Medizinal-Zeitung* 1912, No. 40, p. 729.

Lewin, *Medizinische Klinik* 1912, No. 3, p. 95.

Rost, *Medizinische Klinik* 1912, No. 3, p. 129.

Levy, *Berliner klinische Wochenschrift* 1912, No. 4, p. 191.

Strassmann, *Deutsche medizinische Wochenschrift* 1912, No. 3, p. 108.

Foerster, *Münchener medizinische Wochenschrift* 1912, No. 5, p. 248.

Schenk, *Deutsche Medizinal-Zeitung* 1912, No. 6, p. 81.

Ohlemann, *Wochenschrift für Therapie und Hygiene des Auges* 1912, No. 19, p. 157.

Mendel, *Deutsche medizinische Wochenschrift* 1912, No. 7, p. 339.

Hirschberg, *ibidem*.

Harnack, *Deutsche medizinische Wochenschrift* 1912, No. 8, p. 358.

Grunow, *Medizinische Reform* 1912, No. 2. — *Deutsche Medizinal-Zeitung* 1912, No. 14, p. 243.

Völtz, *Medizinische Klinik* 1912, No. 17, p. 697. — *Biochemische Zeitschrift* 1912, Vol. 40, p. 15.

Keferstein, *Zeitschrift für Medizinalbeamte* 1912, No. 7.

Kühn, *ibidem*.

Bürger, *Wochenschrift für Therapie und Hygiene des Auges* 1912, No. 30, p. 250. — *Berliner klinische Wochenschrift* 1912, No. 36, p. 1705.

Pick, *Berliner klinische Wochenschrift* 1912, No. 19, p. 888.

Schmiedeberg, *Therapeutische Monatshefte* 1912, No. 5, p. 329.

Buchka, *Klinisch-therapeutische Wochenschrift* 1912, No. 23, p. 674.

— *Berliner klinische Wochenschrift* 1912, No. 45, p. 2128.

Rühle, Kroeber, Schlichting, Langgaard, Lennhoff, Stadelmann. For all details, reference should be made to the original communications of these authors, as they cannot be considered here. It may, however, be noted that they show that methyl alcohol itself, when habitually used, or when taken in a single large dose, may act as a poison, so that the toxicity is not due to the presence of impurities in the preparation. The fact that some persons are able to take comparatively large doses of methyl alcohol without apparent harm does not militate against the toxicity of methyl alcohol. It is impossible to say beforehand how large a dose will display an injurious action. According to Rühle, the lethal dose varies between 50 and 100 grammes, but the toxic dose is much less, and blindness may ensue after doses of only 7 to 8 grammes.

The question of treatment is therefore of importance in cases of poisoning, as soon as a reliable diagnosis has been made. When once severe toxic symptoms have supervened, however, treatment will scarcely be of any assistance. Action must therefore be taken as soon as methyl alcohol poisoning is suspected. According to Foerster, the aim of the treatment adopted must be to find ways of eliminating the poison from the system as rapidly as possible. Recourse will therefore be had to hot-air baths, copious draughts of fluids, diuretics, violent exercise, deep breathing in a well ventilated room, saline infusion, venesection, and finally transfusion. Foerster considers ordinary rest in bed to be dangerous.

With regard to tests for methyl alcohol, several suggestions have been made which are of interest to the analytical chemist:

In order to demonstrate the presence of methyl alcohol in commercial preparations of spirit, according to Hellriegel, fractional distillation is first performed, as methyl

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Rühle, Münchener medizinische Wochenschrift 1912, No. 18, p. 964.

Kroeber, Pharmazeutische Zentralhalle 1912, No. 30, p. 825.

Schlichting, Medizinische Klinik 1912, No. 32, p. 1316.

Langgaard, Berliner klinische Wochenschrift 1912, No. 36, p. 1704.

Lennhoff, Soziale Hygiene und praktische Medizin 1912, No. 3.

Stadelmann, Zeitschrift für ärztliche Fortbildung 1912, No. 16 and 17.

Foerster, Münchener medizinische Wochenschrift 1912, No. 16, p. 862.

Hellriegel, Pharmazeutische Zeitung 1912, No. 1, p. 7.

alcohol boils at  $65^{\circ}\text{C}$ . and ethyl alcohol at  $78^{\circ}\text{C}$ . The first fraction is taken for further investigation. It is dehydrated as far as possible by means of calcium oxide and distilled. Oxalic acid dried at  $100^{\circ}\text{C}$ . is dissolved in the distillate, the solution is boiled for about an hour and then left to cool. The oxalic dimethylester which separates has, when dried, a melting point of  $54^{\circ}\text{C}$ . If the alcohol to be tested is of high percentage, the procedure suggested by Reichardt may be adopted. For this purpose, 1 c.c. of caustic soda solution (15 p.c.) is added to 2.5 c.c. of the alcohol to be tested and 3 drops of a 1 p.c. solution of sodium alizarin-sulphonate. To the clear, bluish-violet solution 0.3 to 0.35 gramme of dried oxalic acid is added, and the mixture is well shaken. If ethyl alcohol is present, the colour remains unchanged, but in the presence of methyl alcohol a dirty violet, gelatinous mass is formed, which adheres to the test tube and in a short time turns yellow.

The favourite method of testing for methyl alcohol is based upon the oxidation of methyl alcohol to formaldehyde, which is demonstrated by means of a colour reaction. According to Sailer 0.1 gramme of chromic acid and 10 drops of concentrated sulphuric acid are added to 5 c.c. of the alcohol to be tested. As soon as this mixture has assumed a green colour, 6 drops of it are transferred to a porcelain dish and 20 drops of concentrated sulphuric acid and a little morphine are added. Traces of methyl alcohol or formaldehyde can be recognised by the appearance of a deep yellowish-brown colour, small amounts by a deep crimson-red colour, and large amounts by a deep violet colour. In place of morphine, a few drops of a freshly prepared solution of pyrogallol (0.5:10) may be used. If much methyl alcohol is present, a chocolate-brown colour is produced. A similar method is described by Güth. It is based upon the fact that the alcohol in question, or the material enriched by fractional distillation, is oxidised by sulphuric acid and potassium permanganate. The colourless solution is then tested by the addition of sulphuric acid and a 2 p.c. morphine hydrochloride solution. A violet coloration signifies a positive reaction.

Reichardt, Pharmazeutische Zeitung 1912, No. 4, p. 33, No. 14, p. 134.

Sailer, Pharmazeutische Zeitung 1912, No. 17, p. 165.

Güth, Pharmazeutische Zentralhalle 1912, No. 3, p. 58.

Voisenet oxidises with potassium bichromate or manganese peroxide and sulphuric acid. If hydrochloric acid is made to act upon the product of oxidation, containing a little albumin and nitrous acid, a violet coloration is produced in the presence of methyl alcohol or its oxidation products (formaldehyde or methylal) (compare Voisenet's test for formaldehyde in Merck's Reagenzien-Verzeichnis 1908, p. 269).

The test described by Aufrech t is also based upon the oxidation of methyl alcohol to methylal. It is carried out by diluting 30 c. c. of the material, which has undergone fractional distillation, with 100 c. c. of water; the fluid is cooled and 20 grammes of concentrated sulphuric acid and 10 grammes of potassium bichromate are added; after having stood for several hours, 20 to 30 c. c. are distilled off. The distillate is mixed with 10 times its volume of water, and 10 c. c. are heated to 70° C. with 1 c. c. of sulphuric acid and 2 c. c. of dimethyl-aniline for 5 hours. The mixture is then rendered alkaline, the excess of dimethyl-aniline driven off by steam, and the fluid which remains is acidified with acetic acid and oxidised by means of lead peroxide. If methyl alcohol is present, it is transformed into methylal by the oxidation with chromic acid, and this, when treated with dimethyl-aniline, is converted into tetramethyl-diamido-diphenyl-methane. When this is oxidised by lead peroxide, it assumes an intense blue coloration, which becomes still more intense on heating, while the blue colour produced by ethyl alcohol, or its oxidation products, disappears on heating.

An odour test is recommended by Sailer. In order to avoid errors, it is always advisable in his method to carry out a control experiment. 0.5 gramme of sodium salicylate is placed into each of two wide-necked Erlenmeyer flasks of a capacity of 100 c. c. To one flask 1 gramme of pure ethyl alcohol is added, and to the other flask an equal quantity of the alcohol to be tested. When solution has taken place, 5 drops of concentrated sulphuric acid are dropped into each flask, and this is repeated 4 times at intervals of a minute. About one minute after the last addition of sulphuric acid, if methyl alcohol is present, a distinct odour of

Voisenet, Journal de pharmacie et de chimie 1912, I, p. 240.

Aufrech t, Der Apotheker im Drogenfach 1912, No. 2. — Pharmazeutische Zeitung 1912, No. 4, p. 33.

Sailer, Pharmazeutische Zeitung 1912, No. 10, p. 93.

salicylic methyl ester becomes evident. After the further addition of 0·4 gramme of calcium oxide in 2 c. c. of caustic soda solution, a more pronounced odour is produced, more like that of methyl-phenyl ether.

With regard to the qualitative tests for methyl alcohol, reference may also be made to the communications of Kühl and Aweng. A quantitative estimation of methyl alcohol has been described by W. Koenig.

### Aleudrin.

The carbaminic ester of  $\alpha\alpha$ -dichloro-isopropyl alcohol,  $(CH_2Cl)_2CH \cdot COONH_2$ , forms white crystals, melting at 82° C. It is soluble in alcohol, ether, chloroform, benzol, acetone, glycerin and fatty oils. In water, at the ordinary temperature, aleudrin only dissolves in the proportion of 0·75:100, rather more readily in water containing glycerin.

The earliest experiments with this new drug, which is said to be of therapeutic value on account of its sedative and hypnotic action, were carried out by Th. A. Maass. Pharmacological investigations have shown that it possesses a hypnotic action on cold-blooded and warm-blooded animals, but has practically no influence upon temperature, circulation and respiration. Trials on man have shown that doses of 0·5 gramme ( $7\frac{1}{2}$  grains) usually have a marked sedative action and frequently alleviate any painful conditions which may be present, while doses of 1 gramme (15 grains) produce several hours of sleep. Sleep ensues after a preceding feeling of weariness, and on awaking the patient feels clear in mind and refreshed. In the presence of pain, larger doses are required. In one case a dose of 3 grammes (45 grains) was given without causing any secondary effects.

According to R. Topp, 1 to 1·5 grammes (15 to 24 grains) were required on an average to produce sleep; smaller doses were insufficient. The sleep lasted 4 to 7 hours; usually a feeling of weariness ensued 20 to 30 minutes after taking the drug, which quickly passed into quiet sleep. Three cases proved entirely refractory, one of cerebral syphilis, one of

Kühl, Pharmazeutische Zeitung 1912, No. 34, p. 341.

Aweng, Apotheker-Zeitung 1912, No. 17, p. 159.

Koenig, Chemiker-Zeitung 1912, No. 109, p. 1025.

Maass, Deutsche medizinische Wochenschrift 1912, No. 26, p. 1232.

Topp, Berliner klinische Wochenschrift 1912, No. 47, p. 2230.

cerebral tumour and one of tuberculous meningitis, in which, on account of headache, aleudrin did not produce a satisfactory analgesic and hypnotic action. The preparation was useful, on the other hand, in neuralgia, lightning pains of tabes, maniacal conditions of excitement in alcoholic delirium and conditions of excitement consequent upon the cure of drug habits. To obtain a sedative action in these cases, 0·3 grammie (5 grains) are given 3 times a day. R. Flamm also obtained satisfactory results with aleudrin in maniacal depression, phobia, dementia praecox, melancholia and senile dementia. In severe cases of depression and conditions of fear, a satisfactory action is also obtained by divided doses, and it has the additional advantage of being devoid of cumulative action. It may therefore be safely given for a prolonged period. It is also very useful in the treatment of conditions of extreme excitement, at any rate as a temporary substitute for narcotics, provided it is given in time and in doses of 3 to 4 tablets of 0·5 grammie ( $7\frac{1}{2}$  grains) each.

Gutowitz obtained similar results. He administered up to 2 and 3 grammes (30 to 45 grains) without ill effects in suitable cases. In one case of epilepsy aleudrin proved unsuccessful.

### Alizarin.

To ascertain the keeping properties of a specimen of milk, and the rate and manner of decomposition, W. Morres suggests the employment of the alizarin-alcohol test (alizarol test.) The necessary reagent is prepared by dissolving sufficient alizarin (in the form of paste) to produce a dark reddish-brown, clear solution. 2 c. c. of this, mixed with 2 c. c. of normal milk, should give an intense violet-red colour, resembling the colour of red clover or of heather. With milk of varying degrees of acidity, alizarin solution, like pure 68 p. c. alcohol, gives a flocculent precipitate, and at the same time eight distinct tints varying with the degree of acidity, viz., lilac-red, pale red, brownish-red, reddish-brown, brown, yellowish-brown, brownish-yellow, and yellow. These tints show a degree of acidity of 7·0 to

Flamm, Deutsche medizinische Wochenschrift 1912, No. 49, p. 2311.  
Gutowitz, Medizinische Klinik 1912, No. 47, p. 1911.

Morres, Zeitschrift für Untersuchung der Nahrungs- und Genussmittel 1911, Vol. 22, p. 459.

16 according to Soxhlet-Henkel. If the change of colour from lilac-red to yellow keeps pace with the increase of flocculi, it denotes the presence of a purely lactic acid fermentation. But if the colour does not change from lilac-red, in spite of the appearance of a flocculent coagulation, and in the presence of thick flakes at most turns a darker red, without passing to brownish or yellowish, this is a proof of a purely rennet fermentation. Mixed fermentation, which frequently occurs in summer, can also be recognised by the method described.

### Allantoin.

Allantoin,  $C_4H_6N_4O_3$ , forms white crystals, which are decomposed on heating to about  $200^{\circ} C.$ , without melting. The preparation dissolves with difficulty in cold water, rather more readily in hot water (about 1:30). One way of preparing it synthetically is by the oxidation of uric acid. It can also be isolated from allantoic and amniotic fluid. It was found by E. Schulze and J. Barbieri in vegetable tissues, namely in the shoots of plane trees; and recently it has been found by Ch. J. Macalister, A. W. Titherley and N. G. S. Coppin in the root of *Symphytum officinale*. It is well known that this plant has been used since olden times externally as an astringent in the treatment of wounds, and internally for gastric catarrh, diarrhoea and hæmoptysis. Recently, Bramwell has confirmed the utility of the plant. He applied dressings soaked with an extract prepared from the root of *Symphytum* to chronic ulcers which had resisted all other forms of treatment. The result was surprisingly good. In a case of pruritus ani, also, the drug proved useful, when applied in the form of mucilage. Internally, it proved beneficial in certain cases of gastralgia accompanied by irritation of the mucous membrane.

As Macalister found about 0·8 p. c. of allantoin in the root of *Symphytum*, he decided to test this body therapeutically, as the efficacy of comfrey root might possibly be attributable to it. He found it to be most beneficial

Schulze - Barbieri, *Journal für praktische Chemie* 1882, Vol. 25, p. 145.

Macalister, Titherley, Coppin, *Brit. Med. Journ.* Jan. 6, 1912; see also *Brit. Med. Journ.* Jan. 13 and March 23, 1912. — *Pharmaceutical Journal* 1912, I, p. 91.

Bramwell, *ibidem*.

in ulcers and burns. Its internal administration in ulcers of the stomach and duodenum also gave most encouraging results. The author used 0·3 to 0·4 p. c. solutions, details of the dosage are not given.

### Allosan.

F. Wolf reports his results with allosan. He prescribed it in some 20 cases of acute and subacute gonorrhœa, both of the pars anterior and of the pars posterior of the urethra, and in cystitis, often complicated by prostatitis, and epididymitis, as well as in acute cases of relapsing chronic gonorrhœa. In chronic gonorrhœa, which has become stationary, the author considers all internal medication to be useless, as in these cases only mechanical or surgical treatment is likely to effect a cure. Besides irrigation with silver preparations, potassium permanganate and mercury oxycyanide, he prescribed 1 gramme (15 grains) of allosan, to be taken 3 times a day; as a result of this treatment the duration of the secretion and of the turbidity of the urine was considerably shortened, while the pain accompanying micturition and nocturnal erections always ceased after a few days. The author is struck by the fact that none of his patients experienced unpleasant secondary effects after taking allosan.

M. Arenstein also obtained satisfactory results with allosan in acute gonorrhœa of both males and females. In every case, after 3 to 4 days' internal treatment, he was able to undertake local treatment. Renal irritation was not observed to occur, even though a careful watch was kept for symptoms, and in only one case had allosan to be discontinued, on account of the presence of a gastric ulcer.

### Almatein.

Almatein can be used, like iodoform, as a plug for bones, as has been reported by Werndorff. The advisability of this method of treatment, however, has recently been questioned. M. Lawrowa has described a case of chronic osteomyelitis of the tibia, in which an almatein bone

Wolf, Therapie der Gegenwart 1912, No. 2, p. 94.

Arenstein, Klinisch-therapeutische Wochenschrift 1911, No. 38, p. 1059.

Werndorff, Merck's Report 1909, p. 101.

Lawrowa, Archiv für klinische Chirurgie 1912, No. 4. — Zentralblatt für Chirurgie 1912, No. 26, p. 886.

plug had been used. After a year, although the anatomical cure was still maintained, the patient suffered from insomnia and intense irritability. As this might have been due to an error in technique, Lawrowa experimented on rabbits, and found that almatein was gradually carried by the phagocytes from the plug into the circulation, where it accumulated in the vessels. From this it may be concluded that almatein, in spite of its well recognised antiseptic action, should only be used with care for human beings in the form under consideration.

### Amido-Azotoluol.

Amido-azotoluol and scarlet red have in recent years been recommended by various writers for promoting the growth of skin\*). K. Scheele has investigated the question of the toxicity of these preparations, and its significance for their clinical employment. He has come to the conclusion that these drugs may be used as heretofore without any fear of danger. Amido-azotoluol has, in his opinion, a better and more rapid action than scarlet red. It is true that if large doses are given to animals, they may occasion slight injury to the kidneys, but these doses are far larger than the amounts used clinically. Although it appears from the literature that an 8 p. c. amido-azotoluol ointment causes no harm, yet the author carried out special experiments, paying particular regard to the renal function, and was able to confirm the harmlessness of this ointment. He is therefore of opinion that it may be recommended as a drug likely to prove of service in the treatment of wounds, by bringing about the more rapid formation of epithelium\*\*).

J. Schopf used an 8 p. c. amido-azotoluol ointment in follicular erosions and ectropia of the cervix and the orifice, and obtained noteworthy results.

### Amido-Sulphonic Acid.

Amido-sulphonic acid (sulphaminic acid) forms colourless crystals, readily soluble in water, of the chemical formula  $\text{NH}_2 \cdot \text{SO}_2 \cdot \text{OH}$ .

\*) Compare Merck's Reports 1908—1911.

Scheele, Dissertation Berlin 1912.

\*\*) Compare the article "Scarlet Red" in this Report.

Schopf, Pester medizinisch-chirurgische Presse 1912, No. 47.

In the treatment of Asiatic cholera, according to R. Emmerich, apart from the administration of potassium permanganate or of colloidal manganese peroxide, amido-sulphonic acid is deserving of special consideration. But while the permanganate treatment is of service both at the commencement of an attack of cholera and in advanced cases, it cannot be recommended as a prophylactic even in the stage of premonitory diarrhoea, for the avoidance of food containing nitrates is a better prophylactic. Besides this, a 0.1 p. c. aqueous solution of amido-sulphonic acid is administered as a beverage in small quantities and at fixed intervals. This method of administration is said to give the best results; or a tablespoonful of a 1 p. c. solution may be given every hour, or a teaspoonful to children. The action of the drug depends upon the fact that it immediately converts the toxin of cholera, nitrous acid, into nitrogen. The practical experiments carried out by Possadsky and Glinski in severe cases of cholera showed that amido-sulphonic acid produces remarkable results, especially when employed in good time. But the preparation should not be administered in a routine manner; it is better always to examine the vomit for nitrous acid (using Griess' test), and to continue, or leave off, the medication according to the results obtained. The specific gravity of the blood and the blood pressure should also be determined daily, in order that intravenous injections of hypertonic saline solution may be given in good time.

#### Anæsthesine.

In acute otitis media and commencing furunculosis of the auditory canal, Hübner recommends the following prescription as an anodyne:

Rp. Anæsthesin.	1.0 gramm (15 grains)
Alcohol absol.	10.0 grammes (3 dr.)
Liq. alum. acet.	2.0 grammes (34 min.)
Glycerin	30.0 grammes ( $\frac{5}{6}$ oz)
D. ad vitr. nigr.	

Sterile strips of gauze are soaked in this solution and are introduced into the auditory canal down to the tympanic membrane. The gauze is moistened 3 to 5 times a day

with the warmed solution, besides which a Priessnitz compress is applied to the diseased ear. By means of this treatment the pain soon ceases and there is no fear of poisoning or corrosion, as when other preparations are used (such as phenol-glycerin). Anæsthesin is also of value in combination with iodol (*ana partes æquales*) with the addition of 1 p. c. of menthol, in the form of insufflations in the dysphagia of tuberculous laryngitis.

#### Antiberiberin.

Antiberiberin is a preparation obtained, according to J. Tsuzuki, from rice bran; it is a black fluid having an acid reaction. It is also issued in various other forms, such as pills and powders.

The preparation was first tested on animals by Tsuzuki, and after its specific action in polyneuritis had been established, it was also used for beri-beri in man, in which it proved of great value.

The author advises internal treatment in mild cases of the disease. By this means the evacuation of the bowels is often hastened, cutaneous hyperæsthesia and paralysis are rapidly diminished, the subjective state of the patient is improved, the rapid pulse and cardiac activity are regulated and the œdema disappears with increased diuresis. If the disease is present in a mild form, it can be completely cured in a few weeks by means of this treatment. The drug may also be injected subcutaneously, and in severe cardiac forms this method alone comes into consideration. A syringeful of a 10 p. c. antiberiberin solution is injected daily. If the cardiac debility is of such a degree as to threaten life, cardiac tonics, such as camphor, should be injected simultaneously in order to gain time for the development of the antiberiberin action. In very severe cases the injection is repeated 3 times daily, or even oftener. This treatment is supplemented by the internal administration of antiberiberin. The injection is free from danger and occasions no pain nor any other reaction, wherefore no contra-indications exist.

The daily dose of the antiberiberin preparations mentioned by the author is as follows: Of the 10 p. c. solution for injection 1 c. c. (17 min.), or if necessary more; of anti-

beriberin powder 6 to 10 grammes (90 to 150 grains); of antiberiberin pills 30 to 45; of antiberiberin capsules 3 to 5; of bran extract 1 to 2 grammes (15 to 30 grains); and of rice-bran powder 8 to 25 grammes (120 grains to  $\frac{5}{6}$  oz). There is no maximum dose.

#### Antimeristem.

Further expressions of opinion on the question of antimeristem treatment of cancer have been made\*) by K. Kolb, Th. Johannsen, Martius, Zenker, von Wasielewski and Wülker. In order to settle finally the discussion as to the value of the drug, Kolb, who has once before deprecated the use of the preparation in view of the results of his investigations, has sought to throw light upon those cases described in the literature as having been benefited by antimeristem, by interrogating the authors themselves. He found that all the reported cases suffered from recurrences, with the exception of the one reported by Jenssen, and that all except one ended fatally. These facts are so antagonistic to antimeristem that Kolb denies any specific action of the preparation. On the other hand, he is of opinion that the pre-carcinomatous area of inflammation is influenced in such a way by the drug as to cause an indirect action on the carcinoma cells.

Johannsen treated 3 cases of cancer with antimeristem. He was unable to confirm either an arrest in the process of the disease or an improvement.

Martius points out that, in spite of Schmidt's assertion to the contrary, inflammatory infiltrations and small abscesses frequently occur at the site of injection. He further reported a case in which each injection created an area of diminished resistance, so that tumour cells migrated from the

\*) Compare Merck's Report 1911.

Kolb, Bericht über die Verhandlungen der deutschen Gesellschaft für Chirurgie, 41. Kongress, April 1912, Berlin. — Zentralblatt für Chirurgie 1912, No. 30, Supplement p. 14. — Klinisch-therapeutische Wochenschrift 1912, No. 50, p. 1462.

Johannsen, Zentralblatt für Gynäkologie 1912, No. 14, p. 426.

Martius, Münchener medizinische Wochenschrift 1912, No. 30, p. 1686.

Zenker, Zeitschrift für ärztliche Fortbildung 1912, No. 20, p. 635.

Wasielewski-Wülker, Münchener medizinische Wochenschrift 1912, No. 8, p. 421.

peritoneum, by way of the lymph spaces, to the site of injection, where they developed into metastases.

Wasielewski and Wölker also record nothing but failures with the preparation. They also challenge the basis of Schmidt's cancer hypothesis, because the repetition of the experiments upon which it was based did not lead to the results which had been obtained by Schmidt.

### Antipyrine.

In order to test experimentally and to confirm the styptic action of antipyrine, Amante carried out experiments on dogs. He removed pieces of various sizes from the liver, and treated the wounds so formed with a 50 p. c. solution of antipyrine in water or normal saline solution. Sections of the liver examined microscopically showed that the solution caused the formation of a firm fibrinous membrane, while the underlying parenchyma remained quite unaltered. An autopsy on the experimental animals showed that the wounded organ, after treatment with antipyrine, did not subsequently give rise to haemorrhage in the peritoneal cavity. Experiments on other organs, such as the spleen, kidney and brain, with the exception of the kidney, gave satisfactory results; in sections of the brain, especially, antipyrine solution called forth the immediate formation of a blood clot.

According to O. Podzahrradzky, antipyrine proved beneficial in painful after-pains, due to violent contractions of the uterus during its involution. As antipyrine is also successfully used as an antispasmodic for uterine cramp and in spasm of the bladder and rectum, it might well be more frequently employed for the above named indication in place of injections of ergotin. In most cases a single dose of 0·5 to 1 gramme ( $7\frac{1}{2}$  to 15 grains) suffices to remove the pains completely.

Seifert and Huillier report upon the occurrence and the treatment of antipyrine exanthemata. In a case of inflammation of the thyroid cartilage with swelling of the larynx, Seifert prescribed irrigation with a solution of 1

Amante, Münchener medizinische Wochenschrift 1912, No. 5, p. 284.  
Podzahrradzky, Wiener medizinische Wochenschrift 1911, No. 50.

Seifert, Wiener klinische Rundschau 1911, No. 10, p. 159.

Huillier, Klinisch-therapeutische Wochenschrift 1912, No. 6, p. 187.

gramme (15 grains) of cocaine hydrochloride and 2 grammes (30 grains) of antipyrine in 10 grammes ( $\frac{1}{3}$  oz) of water twice a day. In spite of the comparatively small dose (2 grammes) (34 min.) of the solution and its external application, the second application was followed by severe itching and the appearance of a rash on both hands. It may be noted that this patient showed a marked idiosyncrasy to antipyrine and had been affected by a similar rash on a previous occasion when antipyrine was administered. Following the application of zinc paste, it disappeared in the course of a week. Huillier gives a detailed description of the occurrence and the diagnosis of the bullous antipyrine exanthemata in the mouth. Treatment consists in the administration of considerable quantities of fluid by mouth, aperients, milk and vegetable diet, painting with a 0·5 to 1 p. c. cocaine solution, gargling with hydrogen peroxide solution, and in obstinate cases, cauterisation of the ulcers with tincture of iodine or chromic acid.

### Aperitol.

Aperitol\*), in the experience of Béla Révész, has proved very valuable as an aperient in transient and chronic constipation. The author especially emphasises the fact that the preparation, while reliable in action, never gives rise to gastric pain. He also points out that after the cessation of aperitol medication, its after-effect is evident for some time. In cases of obstinate constipation, also, the stools were satisfactory, if either on purpose or in error an interval had been allowed to elapse in the administration of the drug. The author mentions as a further advantage of aperitol the fact that patients do not become accustomed to the drug, as they do sooner or later to most other aperients. Révész explains the absence of abdominal pain on administration of aperitol in that one component of the preparation, valerianic acid, is a reliable sedative, which does not affect intestinal peristalsis, while the other component, phenolphthalein, collects a considerable amount of fluid in the intestine, which softens the faeces, so that the intestinal walls are not mechanically irritated. Usually two doses daily of 0·2 gramme

\*) Compare Merck's Reports 1908—1911.

Révész, Wiener klinische Rundschau 1912, No. 40, p. 637.

(3 grains) of aperitol are sufficient, but if necessary 3 to 4 tablets (0.2 gramm [3 grains] each) may be given. The useful properties of aperitol are especially evident in constipation occurring in neurasthenia, colitis, haemorrhoids and nephritis.

### Apocynum, Extract of

Induced by Kraemer's recommendation, A. Weiss has studied extract of apocynum in detail. As the preparation acts on the circulatory apparatus in an analogous way to the substances belonging to the digitalis group, but exact physiological investigations on the subject have not as yet been carried out, the author assumes that the action of apocynum is primarily directed to the cardiac contractions, causing an increase in the volume of the beat. The remainder of the action is directed to the vessels, the aortic pressure rising in consequence of vascular contraction in the splanchnic area. Indeed, according to Weiss, the systolic blood pressure, which is depressed on account of cardiac insufficiency, increases rapidly as a result of the administration of extract of apocynum. Accordingly, the preparation may be prescribed in those cases in which digitalis either fails or is not tolerated. In a case of this description Weiss administered 8 drops of the fluid extract on caster sugar in cachets 3 times a day, with the result that in 48 hours the volume of the pulse was increased, arrhythmia was improved, and, without the employment of any other drug, marked diuresis set in. In 5 days all congestive symptoms had disappeared. In a number of other cases, also, the author obtained such excellent results, that he has called extract of apocynum a "vegetable trocar".

One of the author's experiences deserves special mention, namely the fact that extract of apocynum is very useful as a temporary substitute in the presence of cumulative symptoms caused by digitalis substances. Its own action comes into consideration here as well as the possibility of providing the debilitated heart with a certain degree of rest from digitalis medication, in consequence of which it reacts more promptly to digitalis afterwards.

According to Weiss, an effective dose consists of 8 to 15 drops for a single dose, and 16 to 30 drops for a daily dose, but as much as 15 drops 3 times a day have occasionally been given. He never observed toxic secondary symptoms.

This favourable view of the action of apocynum in congestive conditions finds full confirmation in the communication by Békés. He describes a case of loss of compensation with congestive symptoms of the lower extremities, of the abdomen, stomach and lung, in which digitalis, strophanthus, caffeine and theobromine gave rise to vomiting. Extract of apocynum given twice daily in doses of 10 drops was tolerated, at the end of 3 days the symptoms had considerably improved and the condition of the patient became better than the author had seen it for two months.

### Aponal.

The therapeutic value of this preparation\*) has been discussed in the past year by Yonge, Simonstein, Kürbitz and Buttermilch.

Yonge describes aponal as a mildly acting drug, which gives rise to no unpleasant after-effects and is therefore preferable to sulphonal. He states that the rapidity of its action is especially noteworthy, as the patient usually drops into a light and peaceful sleep in the course of half an hour after taking only 0·5 to 1 gramm (7½ to 15 grains). The drug is indicated in insomnia due to over-exertion, excitement, nervous overstrain and senility, but in the presence of pain its action is ineffectual. For senile insomnia larger doses are required, and in one case the author achieved the desired result with 2 grammes (30 grains). It was also of service in a child, aged 12, suffering from chorea; after doses of 0·75 gramm (12 grains) the patient slept the night through and felt well on awaking.

Békés, Der Bahnarzt 1912, No. 4, p. 32.

\*) Compare Merck's Report 1911, p. 154.

Yonge, Medical Press and Circular 1912, Zentralblatt für die gesamte Therapie 1912, No. 9, p. 494.

Simonstein, Allgemeine medizinische Zentralzeitung 1912, No. 11, p. 133.

Kürbitz, Psychiatrisch - neurologische Wochenschrift 1912, No. 24.

Buttermilch, Allgemeine medizinische Zentralzeitung 1912, No. 20, p. 253.

Simonstein prescribed aponal for insomnia due to nervous overstrain, anxiety, neurasthenia, hysteria, cardiac disease, rheumatism, carcinoma and pulmonary disease, and, with the exception of one case of hysteria, he always obtained quiet sleep by its use. Injurious after-effects, such as headache, gastric trouble and renal irritation never occurred, nor was any objection raised against the taste of aponal. Generally, if there was no pain, doses of 1 gramm (15 grains) proved sufficient. The author administered it in the form of tablets, or in order to hasten the action, in warm tea.

Buttermilch was also satisfied with the hypnotic action of 0·5 to 1 gramm (7½ to 15 grains) of aponal in simple agrypnia. The majority of his patients felt refreshed and strengthened on the following morning, and he only rarely noticed disturbing secondary effects. As a result of his experiments, he also recommends it in nervous muscular pains in neuralgia following influenza, in which it displays a sedative effect lasting for several hours, and in gastric and intestinal disturbances occurring in neurasthenic individuals.

According to Kürbitz, maniacs are not particularly influenced by aponal, nor does 1 gramm (15 grains) of the drug suffice for excitable patients suffering from dementia praecox, while doses of 1·5 to 2 grammes (24 to 30 grains) are frequently beneficial. The author has had the same experience with aponal as with trional, viz., when administered in the evening, the patient wakes about 3 or 4 o'clock in the morning and his restlessness returns. He considers the fact that the action of aponal soon passes off to be an advantage of the drug.

### Arbutin.

Arbutin, the glucoside present in the leaves of *Arctostaphylos Uva ursi*, was introduced into therapeutics by L. Lewin in the eighties of the last century in place of the drug. The author had found that the glucoside was split up in the organism into glucose and hydroquinone, a disintegration in which, according to Grisson, not the blood, but the liver,

Lewin, Archiv für pathologische Anatomie und Physiologie 1883,  
Vol. 92, p. 517.

Compare also Real-Encyklopädie der gesamten Heilkunde 1900,  
Vol. 25, p. 314.

Grisson, Maly's Jahresberichte 1888.

kidneys and musculature are said to take part. The glucose is further oxidised in the organism, while the hydroquinone is only partially oxidised. The remaining part appears in the urine as such or as hydroquinone-sulphuric acid. Lewin founded treatment by arbutin on the antiseptic action of hydroquinone. He himself and other authors, such as Unger, Schmitz and Hedde, obtained very satisfactory results with arbutin in affections of the bladder (cystitis, hæmaturia, etc.). Quite recently Lewin still held the view that arbutin formed a good and useful preparation for the treatment of disorders of the bladder, although others, like Paschkis and Feibes, doubted the therapeutic effect of the glucoside. It can scarcely be assumed that arbutin is totally without action in diseases of the bladder, for since its introduction into therapeutics it has always been used, even though not universally or to any great extent. Finally, its action has not been absolutely proved to be solely due to its product of decomposition, hydroquinone, for this is in part further oxidised in the organism.

R. Bass has recently studied arbutin and its behaviour in the organism. According to him, the appearance of hydroquinone as such in the urine is of no therapeutical value, as it is only observed after doses which might prove harmful to the patient. At least, after doses of 3 to 5 grammes (45 to 75 grains) Bass was unable to detect any free hydroquinone in the urine. Nor can unaltered arbutin be detected in the urine. Only after relatively large doses (0.4 gramme per kilogramme of animal) and subcutaneous administration, could the glucoside be demonstrated in the urine. On the other hand, the author considers arbutin medication to be an absolutely non-poisonous method of administering hydroquinone, for it is not possible in experiments on animals to bring about definite toxic symptoms and still less characteristic phenol convulsions by means of the preparation, like those which occur after quite small doses of hydroquinone. This also agrees with Lewin's statements. He stated that arbutin displays no action on the healthy human organism;

Paschkis, Wiener medizinische Presse 1884, No. 13, p. 396.

Feibes, Dissertation Würzburg 1884.

Bass, Zeitschrift für experimentelle Pathologie und Therapie 1912,  
Vol. 10, p. 120.

for even after doses of 20 grammes he observed no striking symptoms within 48 hours. It is therefore probably not absolutely necessary to fix a maximum dose for arbutin, as has been done. The amounts which have been used did not exceed 1 gramme (15 grains) for a single dose, and 6 grammes (90 grains) for a daily dose. The following prescriptions may be given:

Rp. Arbutin. 3·0 to 10·0 grammes (45 to 150 grains)

Aq. destill. 150·0 grammes (5 oz)

M. Sig.: 3 to 6 tablespoonfuls daily.

Rp. Arbutin 1·0 grammme (15 grains)

Sacch. 0·5 grammme ( $7\frac{1}{2}$  grains)

M. Ft. pulv. Mitte tal. X.

Sig.: 3 to 4 powders daily.

### Argatoxyl.

The value of argatoxyl (atoxylate of silver, argenti atoxylas) in the treatment of puerperal fever is illustrated by J. Hirsch, who has once before reported upon this new preparation\*). He used it, according to the prescription recommended by Eisenberg, in the form of a 10 p. c. oily emulsion given in the form of intramuscular injections. Of 12 cases of puerperal infection, some of them severe, and 3 of which the author describes in detail, 11 were cured. Even though it cannot be proved that these favourable results were directly due to treatment by argatoxyl, yet the author believes that further tests with the drug should be encouraged. He is specially justified in taking this view as the drug in no case showed a harmful effect, nor any action on the heart or lungs. It is true that local abscesses formed at the site of injection in 3 cases, but these healed rapidly after being lanced. The author considers them to be manifestations of local irritation (necrosis), such as may occur after the administration of other preparations of arsenic. The early employment of the remedy, which may be combined with cardiac drugs, such as caffeine, alcohol and digalen, is important for its success. 0·3 to 0·4 grammme (5 to 6 grains) of argatoxyl are given for a single dose. The injections

Hirsch, Deutsche medizinische Wochenschrift 1912, No. 12, p. 560.

\*) Compare Merck's Report 1911, p. 166.

Eisenberg, Merck's Report 1911, p. 167.

must be repeated daily or at intervals of several days, as required.

P. Rosenstein, having obtained a successful result in a case of puerperal fever, was led to test argatoxyl in a number of cases, and was satisfied with his results. His 20 cases consisted of carbuncle, septic cellulitis, septic scarlet fever, peritonitis, puerperal fever, mastitis, otitis media, septic processes of unknown origin and articular rheumatism. The primary disease in every case was accompanied by severe septic infection, in which every other form of treatment failed. Although the injections of argatoxyl caused the formation of an abscess at the site of injection in every case, yet the action of the drug was manifest. The author sought a scientific explanation for the value of the preparation. According to him, its action is due to its bactericidal properties and to the stimulation of leucocytosis. The injection abscess is always sterile.

Zülzer recommends argatoxyl in diagnostically doubtful cases. He himself has used it with good results in several cases of septic infection in endocarditis and pericarditis with double pleurisy, in parotitis with follicular tonsillitis and inflammation of the kidneys and in scarlatinal nephritis. Hirsch and Eisenberg also report upon the satisfactory way in which septic processes are influenced by argatoxyl, while Klemperer observed no action in three severe cases. Blumenthal also had doubtful as well as good experiences with argatoxyl. The drug may also be given intravenously dissolved in a 3 p. c. solution of piperazin, as this solution is not more toxic than the oily emulsion; but this method of administration must be handled with the greatest caution in man.

In the most severe puerperal infections caused by streptococci, W. Kirchhoff made use of silver atoxylate, in one case with no effect and in another case with uncertain effect. As he has been unable to establish either a prophylactic or a curative effect in experiments on animals, and as he

Rosenstein, Zülzer, Hirsch, Eisenberg, Klemperer, Blumenthal,  
Allgemeine medizinische Zentralzeitung 1912, No. 26, p. 338.

Rosenstein, Deutsche medizinische Wochenschrift 1912, No. 41,  
p. 1924.

Kirchhoff, Zeitschrift für Geburtshilfe und Gynäkologie 1912, Vol.  
71, p. 493.

fears the abscess formation at the site of injection, he refuses to give intramuscular injections of the preparation.

### Argentarsyl.

Argentarsyl is a combination of colloid silver and iron cacodylate in the proportion of 0·05 to 10 c.c. This at least is the definition of the preparation given by Barcanovich, who obtained surprising results in malaria by its use. He describes two cases in which a single injection of 10 c.c. of the drug completely cut short severe, acute attacks within 24 hours, without recurrences. His other experiences refer to two years' use of the preparation. As iron cacodylate and sodium cacodylate have also proved beneficial in malaria and have been recommended by others\*), the author's communication should give occasion for further trials.

The action of argentarysyl may be demonstrated by examination of the blood as well as by practical results. Barcanovich did not abstract the blood for examination from the fingertip, as he frequently found it to give inexact results, but took it from a cubital vein. He found that the patient's blood, which contained numerous plasmodia before treatment, was absolutely free from them after an injection. He particularly emphasises the fact that this freedom from plasmodia is not transient, as is usually the case when quinine is employed, but is permanent, so that the patients are immunised as a consequence of the injections. The author regards the feeling of well-being observed in various patients as a proof of convalescence, coupled with the increase in body-weight and the disappearance of the splenic tumours.

### Arsenferratose.

W. D. Nikolskaja reports very good results obtained by treatment with arsenferratose in gynaecological practice. It proved of value in nervousness and anaemic conditions following childbirth and operations, as well as in loss of appetite and general debility. The general health was improved in all cases and the body-weight usually increased. The drug

Barcanovich, Münchener medizinische Wochenschrift 1912, No. 11,  
p. 583.

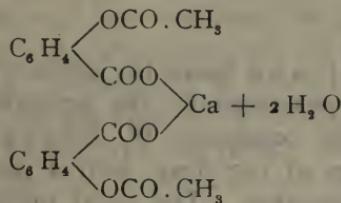
\*) Compare Merck's Report 1910, p. 1-38.

Nikolskaja, Therapeutitscheskoje Oboshrenie 1912, No. 3.

was very well tolerated, except in a few cases which were associated with gastric and intestinal trouble. It is also said to furnish excellent results in paediatric practice. (With regard to dosage, etc., compare Merck's Report 1907.)

### Aspirin.

During the last few years attempts have been made to extend the use of aspirin by preparing it in a more soluble form\*). The calcium salt of acetyl-salicylic acid possesses this advantage, and is put on the market under the name of "soluble aspirin". It is a white powder, readily soluble in water, of the chemical constitution:



In an anhydrous condition, it contains 90 p. c. of aspirin and 10 p. c. of calcium. The advantage of "soluble aspirin" is that it can readily be dissolved, if there should be any difficulty in swallowing powders and tablets, as for example in the case of children. A solution of this kind, however, should not be kept too long, as otherwise the preparation is decomposed with the formation of acetic acid, and the solution which was perfectly tasteless assumes an acid reaction. A further advantage of the new preparation consists in its neutral reaction and in the absence of gastric and oesophageal complications, such as have occasionally been observed after taking aspirin. Finally, it is particularly pointed out by Görges that the calcium contained in the drug prevents the occurrence of renal inflammation.

Görges investigated "soluble aspirin" and found that it gave rise to no secondary effects, while its therapeutic action was identical to that of aspirin. This was the case in acute articular rheumatism, acute endocarditis, pericarditis, pleurisy, influenza, angina, neuralgias and tabetic pains. This

\*) Compare: "Kalmopyrin", Merck's Report 1911 and "Hydropyrin" ibidem 1910 and 1911.

Görges, Deutsche medizinische Wochenschrift 1912, No. 26, p. 1232.

has been confirmed by A. Eulenburg, Dengel, O. Lehmann, Seiler and R. Bercke. Eulenburg suggests the following prescription for the internal administration of the soluble form:

Rp. Aspirini solubilis	8·0 grammes (120 grains)
Aq. destill.	175·0      "      (6 oz)
Syrup. Cerasorum	15·0      "      ( $\frac{1}{2}$ oz)
M. Sig.: 1 tablespoonful	3 to 4 times a day (for children 1 teaspoonful).

Instead of the solution, one tablet may be dissolved in a little water before use; it must be remembered that as the tablets contain starch, they do not yield a clear solution.

### Atophan.

While Weintraud bases the action of atophan upon the specific property possessed by the preparation of eliminating uric acid from the organism, W. Skorczewski seeks to connect the action of the drug with a disturbance of oxidation within the organism. The good results obtained by the use of atophan in therapeutics nevertheless show that it is useful to the organism. But the author suggests a change in the dosage; he believes that at the commencement of atophan administration very small doses should be given, which are not in excess of the uric acid excretion. The treatment may then be prolonged if necessary, and the doses gradually increased. In acute attacks of gout atophan should, in the author's opinion, be discarded; medication should only be commenced when the disease has subsided. He admonishes caution in all cases. Brugsch also believes the part played by atophan in excreting uric acid to be secondary, while its primary action is to be sought in the property possessed

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Eulenburg, Medizinische Klinik 1912, No. 29, p. 1210.

Dengel, Medizinische Reform 1912, p. 320. — Halbmonatsschrift für soziale Hygiene und praktische Medizin 1912, No. 17.

Lehmann, Allgemeine medizinische Zentralzeitung 1912, No. 29, p. 375.

Seiler, Deutsche medizinische Wochenschrift 1912, No. 46, p. 2176.

Bercke, Berliner klinische Wochenschrift 1912, No. 29, p. 1378.

Weintraud, Merck's Report 1911. — Therapeutische Monatshefte 1912, p. 21.

Skorczewski, Wiener klinische Wochenschrift 1911, No. 49, p. 1700, 1912, No. 16, p. 593. — Zeitschrift für experimentelle Pathologie und Therapie 1912, No. 3, p. 501.

by the preparation of mobilising uric acid. Retzlaff likewise opposes the view put forward by Weintraud that it possesses an elective action on the kidneys. For on the one hand, in healthy individuals kept on a purin-free diet (the blood being free from uric acid), he found uric acid in the blood after the administration of atophan, and, on the other hand, in gouty subjects kept on a strict diet, he found no diminution of uric acid in the blood, even after prolonged use of atophan with copious elimination of uric acid. Like other authors, he therefore seeks the action of atophan in the increase of parenteral nuclein metabolism. For the same reasons, Klemperer and Dohrn do not accept Weintraud's hypothesis of the method of action of atophan\*).

Communications on the treatment of gout by atophan have been made by W. Weintraud, Plehn, Retzlaff, E. Tschernikow, Meidner, M. Dohrn, H. Bach and E. Strauss, Th. Brugsch, F. Richter, R. Feulgen, A. Bendix and von Boltenstern. When administered immediately after the first appearance of pain, it often cuts short the attack within a few hours, even if only a few tablets of 0.5 gramme ( $7\frac{1}{2}$  grains) are given. Usually complete success may be obtained by the administration of 1 gramm (15 grains) 3 to 4 times a day, even within 2 to 3 days after the appearance of inflammatory symptoms. But if atophan has been administered for 3 or 4 days without satisfactory result, there is usually no object in continuing the medication. It is then best to leave it off entirely for a few days and to

\*) Compare also Rösler and Jarczyk, Deutsches Archiv für klinische Medizin 1912, Vol. 107, p. 573.

Plehn, Deutsche medizinische Wochenschrift 1912, No. 3, p. 102.

Retzlaff, Deutsche medizinische Wochenschrift 1912, No. 9, p. 404.

— Klinisch-therapeutische Wochenschrift 1912, No. 7, p. 219.

Tschernikow, Russky Vratch 1912, Vol. 11, p. 48.

Meidner, Therapie der Gegenwart 1912, No. 4, p. 164.

Dohrn, Zeitschrift für klinische Medizin 1912, No. 5 and 6, p. 445 and 462.

Bach-Strauss, Münchener medizinische Wochenschrift 1912, No. 31, p. 1714.

Brugsch, Berliner klinische Wochenschrift 1912, No. 34, p. 1597.

Richter, Deutsche medizinische Wochenschrift 1911, No. 51, p. 2364.

Feulgen, Dissertation Kiel 1912.

Hirschberg, Therapeutische Monatshefte 1912, No. 10, p. 721.

Bendix, Therapie der Gegenwart 1912, No. 7, p. 301.

Boltenstern, Deutsche Ärzte-Zeitung 1912, No. 19 and 20.

begin afresh with a daily dose of 3 to 5 grammes (45 to 75 grains). Richter was only able to obtain the desired effect in acute gout in one-third of the cases treated. In opposition to Weintraud, he holds the view that in an acute attack colchicine is the drug of choice, and it has never failed in his hands\*). In an acute attack, in his experience, it cannot be replaced by any other drug. It is administered in doses of 0.001 gramme ( $\frac{1}{64}$  grain) 4 to 6 times in the space of 2 hours, and is said always to be beneficial and never injurious. Richter, on the other hand, found atophan very efficacious in chronic gout, in which no typical attack with inflammatory symptoms occurs. In these cases it is also apparently of diagnostic value, and is certainly superior to other antirheumatic and antineuronalgic drugs, such as aspirin.

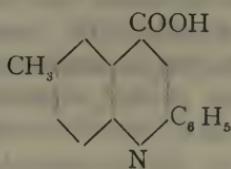
Brugsch only prescribes atophan (2 to 3 grammes [30 to 45 grains] a day) during the acute stage immediately before or after an attack, as uric acid excretion is usually much reduced at this period. He does not give it during the severe joint attacks, as uric acid excretion is normally increased during this period and atophan cannot contribute much towards its further increase. In typical arthritis uratica or primary chronic arthritis uratica, he gives the drug at regular intervals, in daily doses of 2 to 3 grammes (30 to 45 grains) for 2 days every 4 weeks in mild cases, and every 8 to 14 days in more severe cases. The author does not recommend daily administration in these cases. On the other hand, he reports that in polyarthritis urica the patients are able to take 1 to 2 grammes (15 to 30 grains) of atophan daily for a year without affection of the kidneys, the uric acid excretion is increased during the whole period, and if the medication is discontinued, pains recur. In true renal gout the results of atophan treatment were less satisfactory. Here the drug failed in some cases and, in spite of the simultaneous administration of sodium bicarbonate, it frequently gave rise to renal pain and occasionally to vomiting, indisposition, rapid pulse and palpitation. Brugsch therefore considers it to be chiefly indicated in arthritis and in primary chronic arthritis urica, in which it should be administered intermittently; in polyarthritis urica, in which it may be administered for a more or less prolonged period; and in renal gout, in which caution is necessary.

\* ) Compare Merck's Reports 1908 and 1909.

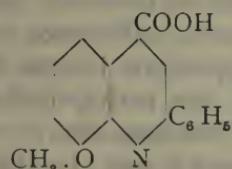
Retzlaff, like Brugsch, considers the best time for administration to be that immediately preceding and succeeding the attack. As a prophylactic measure, he gives 2 to 3 grammes (30 to 45 grains) of atophan daily for 3 days at intervals of a fortnight, a dose which brings about the maximum of uric acid excretion with the minimum amount of medicament, thus attaining the optimum action. In secondary effects, such as cardialgia and heartburn, etc., one quarter to half a teaspoonful of sodium bicarbonate is added to each gramme (15 grains) of atophan.

Atophan is beneficial in acute articular rheumatism as well as in gout, and this is confirmed by Weintraud, Fränkel, Béndix, Oeller and Klempner. Weintraud suggests a daily dose of 3 to 5 grammes (45 to 75 grains). Hirschberg also obtained a good result with the drug in a case of sciatica and chronic proctitis in an old man.

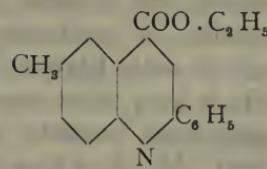
In place of atophan, which possesses a bitter taste, novatophan, which is tasteless, may be used in the same way. It is the ethyl ester of paratophan (methyl-phenyl-quinoline-carbonic acid):



Paratophan



Isatophan



Novatophan

Novatophan forms a yellowish-white, tasteless powder, insoluble in water, soluble in alcohol, ether and benzol. Its melting point is 75° to 76° C. Isatophan (methoxy-phenyl-quinoline-carbonic acid) is also a tasteless preparation, clinically equivalent to atophan and paratophan. It is a yellow, crystalline powder, melting at 216° C. It is insoluble in water, readily soluble in alcohol. It differs from paratophan in being soluble in alkalies.

### Atoxyl.

In order to elucidate the action of atoxyl, L. Arzt and W. Kerl have repeated the experiments originally carried

Oeller, Medizinische Klinik 1912, No. 50, p. 2029.

Arzt-Kerl, Wiener klinische Wochenschrift 1912, No. 38, p. 1408.

out by Levaditi. As is well known, the method of action of atoxyl is still under discussion. Thus, according to Ehrlich, the action of atoxyl on trypanosomes is due to the reduction of the preparation and to the products of reduction; but, according to Levaditi, the action only takes place with the coöperation of hepatic albumin, an arsenic-free, trypanocidal toxalbumin, the so-called "trypanatoxyl", being formed. Other authors attribute the action of atoxyl to the formation in the organism of arsenious acid\*), or assume that reduction and oxidation occur simultaneously, and that the inorganic arsenic thus liberated destroys the trypanosomes. The action of atoxyl has also been sought in the production of the antibodies to which it gives rise\*\*). Finally, it is open to question whether or not atoxyl itself possesses a trypanocidal action.

The experiments of Arzt and Kerl prove that a toxic substance is really produced through the influence of an organ emulsion. Liver emulsion, in particular, raises the toxicity of atoxyl; brain emulsion does so to a less degree. Glycogen acts in a similar manner, whereas lecithin, cholesterol and nuclein, used in place of liver emulsion, are not capable of producing toxic substances. Possibly this result agrees with Ehrlich's hypothesis in that the organ substances which have been named, and perhaps others as well, represent substances capable of reducing atoxyl. But, on the other hand, M. Rothermundt and J. Dale have succeeded in proving that atoxyl in an unaltered form possesses trypanocidal properties. This was confirmed *in vitro* in nagana, dourine and mal de Caderas, provided certain experimental conditions were observed. But the action takes place slowly and is dependent upon the temperature. The authors did not succeed, however, in killing spirochetes and spirilla of fowl, either *in vitro* or *in vivo* by means of atoxyl. These results

Levaditi, Comptes rendus de la société de biologie 1908, Vol. 65, p. 23, 1909, Vol. 66, p. 33.

Ehrlich, Verhandlungen der deutschen dermatologischen Gesellschaft Frankfurt 1910.

\*) Compare Blumenthal and Jacoby, Biochemische Zeitschrift 1909, Vol. 16, p. 20. — Breinl und Nierenstein, Zeitschrift für Immunitätsforschung 1909, p. 620.

\*\*) Compare So, Wiener klinische Wochenschrift 1911, p. 452. Rothermundt-Dale, Zeitschrift für Immunitätsforschung 1912, p. 565.

are opposed to those of S. Peschics who, by means of suitable doses, was able to free his experimental animals, affected with chicken spirillosis, from the parasites several times in succession.

C. P. White and A. E. Woodall tested the pharmaceutical action of atoxyl in carcinoma of mice, and found that subcutaneous doses of 0·05 grammes of atoxyl cause the disappearance of small tumours, while larger tumours remain unaffected or their growth is only slightly retarded.

F. D. Boyd, in experiments on man, found that intramuscular injections of atoxyl (0·35 gramme) cause a retardation in the albumin metabolism. At any rate, there was a considerable decrease in the nitrogen excretion in the urine, which was manifested by a decrease in urea and less so by a decrease in creatinin and uric acid. There was no alteration in the excretion of ammonia salts.

W. L. Yakimoff reports upon the results of atoxyl treatment in veterinary medicine, in experimental dourine and chronic heat of horses. According to these results, atoxyl appears to be a promising remedy for dourine, by means of which this disease, formerly so difficult to treat, may be cured. After the first few subcutaneous injections, cutaneous plaques and swelling of the sexual organs disappear and do not recur. Only in two horses, in which the trypanosomes had probably developed resistance to atoxyl at the beginning of treatment, were recurrences observed, which only yielded completely to combined treatment by atoxyl and corrosive sublimate. The author occasionally observed an undesirable secondary effect of atoxyl treatment, namely changes in the eyes.

H. Spude has adopted atoxyl in combination with a method of electromagnetic stimulation for the treatment of cancer. Into the tumour and its immediate neighbourhood he injected black ferrous oxide in suspension and acted upon it by means

Peschic, Zeitschrift für Immunitätsforschung 1912, Vol. 13, p. 364.  
White-Woodall, Medical Chronicle 1912, Vol. 56, p. 185.

Boyd, Archives internationales de pharmacodynamie et de thérapie 1911, Vol. 21, p. 281.

Yakimoff, Zeitschrift für Infektionskrankheiten der Haustiere 1911, Vol. 9, p. 307 and 3921. — Berliner tierärztliche Wochenschrift 1912, No. 10, p. 172.

Spude, Münchener medizinische Wochenschrift 1912, No. 31, p. 1713.

of an alternating current magnet. The healing tendency induced by this stimulation was supported by intravenous injections of 0·1 to 0·2 grammes ( $1\frac{1}{2}$  to 3 grains) of atoxyl. By this method the author obtained good results in two cases of cutaneous cancer, which had persisted for over a year.

### Atropine Sulphate.

According to Umber, there are two chief factors to be considered in the treatment of phosphaturia. The one, which is manifested by too high a proportion of earthy alkalies, calcium salts and magnesium salts in comparison with the phosphoric acid excreted, is treated by a diet as poor as possible in lime; the other, recognised by too low a degree of acidity of the urine, can be favourably influenced by treating the gastric hypersecretion, so often associated with phosphaturia. For this purpose atropine is used, with which the author has, for a number of years, obtained very good results in the most obstinate cases. In consideration of a possible super-sensitiveness to atropine, 0·0005 gramme ( $\frac{1}{125}$  grain) is given for a first dose, and in the course of a few days the dose is increased to 0·003 gramme ( $\frac{1}{20}$  grain), which is taken in separate doses of 0·001 gramme ( $\frac{1}{64}$  grain) after meals. The highest dose reached is continued for a fortnight, after which the dose is gradually reduced. Should phosphaturia recur, the treatment may be repeated. It is supported by general tonic treatment.

On Forchheimer's recommendation, O. Mosenthal administered large doses of atropine in diabetes mellitus, but was unable to confirm this author's good results, even when he gave definitely toxic doses. The excretion of sugar remained uninfluenced.

K. Fluss investigated Schindler's statements with regard to the value of atropine in gonorrhœa. Atropine, as is well known, is thought to supplement the treatment of gonorrhœa with silver, by guarding against complications. In 138 cases of male gonorrhœa the author was able to confirm

Umber, Therapie der Gegenwart 1912, No. 3, p. 97.

Mosenthal, Journal of the American Medical Association 1912, Vol. 58, p. 777.

Fluss, Dermatologische Wochenschrift 1912, p. 192.

Schindler, Berliner klinische Wochenschrift 1909, No. 37.

Schindler's good results, and he therefore recommends further trials\*).

Dorner reports upon the treatment of the status epilepticus. In the absence of a reliable remedy, he suggests the employment of atropine in large doses; it acts as a narcotic, regulates the bowels and stimulates the heart. In his experience, epileptics will tolerate 5 times the maximum dose. These large doses are said occasionally to cut short the status epilepticus completely, and frequently to render it less severe and to diminish the frequency of its occurrence; thus danger to life is eliminated. In a severe seizure, Dorner has given subcutaneous injections of 0.003 grammes ( $\frac{1}{20}$  grain) of atropine sulphate 2 to 3 times in the space of 24 hours, and has thus inhibited the attack. Atropine is also of value in ordinary epilepsy, in which a solution of 0.03 grammes ( $\frac{1}{2}$  grain) of atropine sulphate in 10 grammes ( $\frac{1}{3}$  oz) of water may be prescribed in separate doses of 10 to 20 drops, together with preparations of bromine.

Finkelburg has contributed to the knowledge of the action of atropine on the heart. He reports the case of a patient who had suffered from cardiac irregularity for 15 years. The author injected 0.001 grammes ( $\frac{1}{64}$  grain) of atropine sulphate; 20 minutes later only a few extra systoles were noted, and after 30 minutes the normal pulse beats predominated. After  $2\frac{1}{4}$  hours the atropine action had passed off and the intermittent pulse returned.

G. Singer points out that, as a rule, in spastic constipation the rectal application of atropine gives better results than does its internal use. In these cases very small doses usually suffice to mitigate the trouble and to call forth a prompt action of the bowels. Even if extract of belladonna is employed, suppositories containing 1 to 1.5 centigrammes ( $\frac{1}{6}$  to  $\frac{1}{4}$  grain) of the extract are sufficiently strong. Those nervously constituted individuals, who are almost continuously troubled with spasm of the colon, appear to react very strongly to atropine, so that even small doses of atropine give rise to the well known secondary effects, such as disturbance of ac-

\*) Compare Merck's Report 1910, p. 119.

Dorner, Allgemeine Zeitschrift für Psychiatrie Vol. 69, No. 1.

Finkelburg, Medizinische Klinik 1912, No. 14, p. 584.

Singer, Deutsche medizinische Wochenschrift 1912, No. 23, p. 1085.

comodation, dryness of the throat and hoarseness. In intestinal obstruction, on the other hand, doses of atropine sulphate larger than the maximum dose are requisite (3 to 5 milligrammes) ( $\frac{1}{20}$  to  $\frac{1}{12}$  grain) in order to effect complete paralysis of the violently contracting muscles and thus cause evacuation of the intestinal contents.

After the employment of atropine ointment, G. Weill has observed eczema of the eye-lids, which disappeared when the treatment was discontinued, and reappeared when the application was renewed. He attributes this phenomenon to anaphylaxis rather than to idiosyncrasy.

According to S. Weissenberg, atropine is beneficial in many cases of buzzing in the ears without recognisable cause. The following prescription is employed:

Rp. Sol. Atropin. sulph. 0·01:15·0.  
Sig.: 10 to 15 drops three times a day.

**Barium Sulphate puriss.**, free from phosphoric acid and nitric acid, for Röntgen ray diagnosis.

Barium sulphate\*), suggested by P. Krause for Röntgen ray diagnosis, has been adopted in many clinics on account of its cheapness and safeness. Further communications with regard to its use have been made by Günther and Bachem, Nieden, Groedel and Levi, Schwarz, Bensaudé and Ronneaux, Holst and Schlesinger and Peyer.

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Weill, Klinische Monatsblätter für Augenheilkunde 1912, p. 458.  
Weissenberg, Deutsche medizinische Wochenschrift 1912, No. 48, p. 2273.

\*) Compare Merck's Report 1911.

Günther-Bachem, Zeitschrift für Röntgenkunde 1910, Vol. 12, p. 369.  
— Deutsche medizinische Wochenschrift 1911, p. 717.

Bachem, Berliner klinische Wochenschrift 1912, No. 30, p. 1425.  
Nieden, Deutsche medizinische Wochenschrift 1911, No. 33, p. 1515.  
Groedel-Levi, Fortschritte auf dem Gebiet der Röntgenstrahlen Vol. 17, p. 55.

Schwarz, Wiener medizinische Wochenschrift 1912, No. 16. —  
Berliner klinische Wochenschrift 1912, No. 16, p. 726, No. 30, p. 1424.

Bensaudé-Ronneaux, Presse médicale 1911, p. 520. — Merck's Report 1911, p. 170.

Holst-Schlesinger, Münchener medizinische Wochenschrift 1912, No. 6, p. 312.

Peyer, Zeitschrift für Röntgenkunde 1912, Vol. 14, p. 41.

These publications show conclusively that really pure barium sulphate, free from soluble barium salts, is a safe substance, which is eminently suitable as a shadow-forming medium for Röntgen ray examinations. The best proof of this is the fact that it has been used in thousands of cases with good results and with no untoward consequences. Barium sulphate puriss. for Röntgen ray diagnosis, prepared by me and carefully tested, is recognised as a reliable preparation of barium sulphate. By means of this preparation, the mixtures with cornflour or other vehicles suggested by various authors can readily be prepared; it is not advisable to use ready made mixtures, as the chemical test is then difficult. It is advisable to obtain the barium sulphate for internal use from the pharmacist under the definite designation "Barium sulphate puriss. for Röntgen ray diagnosis", for thus a guarantee is given of its purity and utility. If "for Röntgen ray diagnosis" or "for internal use" is always added, the danger of mistaking it for barium sulphide will be avoided; even if abbreviations are used, which in this case are better omitted. As no satisfactory method of testing barium sulphate has as yet been published, I have contributed one to various scientific journals for the benefit of those interested. To insure its further circulation, it may be reproduced here:

Barium sulphate puriss. is a fine, white powder, almost insoluble in water and dilute acids. — If a solution of 5 grammes of sodium carbonate crystals in 15 c.c. of water is boiled for about 1 minute with 1 gramme of barium sulphate, then filtered and after adding an excess of hydrochloric acid to the filtrate, barium chloride solution is added, a white precipitate is produced. The precipitate remaining on the filter is washed off with water and dissolves partially in nitric acid. The solution thus obtained gives a white precipitate with dilute sulphuric acid. — 10 c.c. of acetic acid (sp. gr. 1.064) and 90 c.c. of water are heated to boiling with 10 grammes of barium sulphate and filtered. 50 c.c. of the filtrate are evaporated to dryness on a water bath. (It is inadmissible to use the filtrate itself in testing for barium.) The residue is treated with 20 c.c. of water and the solution filtered. If a few drops of dilute sulphuric acid are added to the filtrate, no separation of barium sulphate should occur within an hour. (This test would also reveal the presence of barium carbonate and soluble barium salts.) — 25 c.c. of the acetic

acid extract should remain unaltered on the addition of solution of sulphuretted hydrogen. (Heavy metals.) — If 10 c. c. of nitric acid (sp. gr. 1.149—1.152) are heated to boiling with 2 grammes of barium sulphate and filtered, the addition of ammonium molybdate solution to the filtrate should not cause the separation of a yellow precipitate within an hour. (Barium phosphate.) — If 2 grammes of barium sulphate are rubbed up with 10 c. c. of stannous chloride solution the mixture should not assume a darker colour within an hour.

Barium sulphate destined for internal use must satisfy these requirements.

### Benzoic Acid.

G. W. Morey determined experimentally that pure, sublimed benzoic acid might be usefully employed in acidimetry as a standard substance. For this purpose, the acid is heated to 140° C. in a covered platinum crucible; on cooling it is broken up into small pieces, which are kept in a little weighing bottle. Benzoic acid prepared in this way is said to possess the advantage of remaining unchanged, so that it need not be dried before use. As a large amount can be weighed at a time, the errors of weighing are reduced. Phenolphthalein is used as indicator. An alcoholic solution of benzoic acid is prepared for titration.

### Benzol.

Induced by Selling's experiments, A. von Korányi investigated the effect of benzol on the constitution of the blood and on the course of leukæmia. He came to the conclusion that the drug exerts a beneficial effect on the morbid condition of the blood in this disease. The chief effect consists in a reduction in the number of the white blood corpuscles and after a time in an increase of the erythrocytes; and also in the reduction of the splenic tumour and an improvement in the general health. The result appears to be equally good in all forms of leukæmia. It takes place more slowly than in treatment by X rays, but it is efficacious in cases in which this fails. However, patients treated by X rays

Morey, Chemical News 1912, Vol. 106, p. 63. — Journal of the American Chemical Society 1912, Vol. 34, p. 1027.

Selling, Ziegler's Beiträge 1911, Vol. 51, p. 576.

Korányi, Berliner klinische Wochenschrift 1912, No. 29, p. 1357.

apparently react more rapidly to benzol. Small doses appear to stimulate leukopoiesis and the author therefore advises the employment of large doses. Daily doses of 3 to 4 grammes (44 to 60 min.) are usually well tolerated for months, though troublesome secondary effects, such as heartburn, eructations, transient tracheo-bronchitis and vertigo may occur. Gastric troubles may be avoided by the simultaneous administration of oil, and if vertigo supervenes, the doses must be reduced.

In a case of polycythaemia with splenic tumour, the administration of benzol also proved beneficial.

G. Kiralyfi was on the whole able to confirm this author's favourable experiences. In his opinion, benzol is best given in gelatin capsules (containing 0.5 gramme of benzol and 0.5 gramme of olive oil), of which 4 a day are given at first, and the number is gradually increased until 2 capsules are taken 5 times a day. They should be taken on a full stomach. The author is unable to give particulars as yet as to the duration of the good result. Benzol administration has the advantages of simplicity and safety as compared with X ray treatment, but on account of the necessity of frequent blood examinations, it is for the present limited to use in hospitals.

Tedesko and B. Stein each report a case of lymphatic leukæmia, in which benzol treatment was employed with success.

### Bismuth Subnitrate.

The treatment of fistulas by means of Beck's bismuth paste\*) has been the subject of a number of publications during the past year. Beck, the author of the method, still believes firmly in the harmlessness and the great utility of bismuth paste. In a recent paper he points out that the paste forms a good medium for representing the course of the fistulas by means of X rays. It is claimed that no other method has the same diagnostic value. It offers such an ac-

Királyfi, Wiener klinische Wochenschrift 1912, No. 35, p. 1311.  
Tedesko, Münchener medizinische Wochenschrift 1912, No. 48, p. 2653.

Stein, Wiener klinische Wochenschrift 1912, No. 49, p. 1938.

\*) Compare Merck's Reports 1908—1911.

Beck, Wiener medizinische Wochenschrift 1912, No. 5. — Deutsche Medizinalzeitung 1912, No. 10, p. 162.

curate picture that surgical treatment can be carried out according to a definite plan and that operable cases can be distinguished from inoperable cases. The diagnosis is invaluable for rectal fistulas, as with its help useless operations can be avoided. At the same time, the curative value of bismuth injections comes into consideration, for they will cure both operable and inoperable cases of rectal fistulas. According to Beck, operation should only be undertaken in those cases which have resisted treatment by bismuth paste. As this is practically painless, free from danger and successful in at least 75 p. c. of the cases treated, it should always be given a trial before operating. In order to carry out the application of bismuth, the patient is placed in the knee-elbow position, the opening of the fistula is cleansed with alcohol, and the bismuth paste, which has been liquefied by placing in hot water, is injected by means of a warmed metal syringe. Too great pressure should not be used; after the injection, the patient should only experience a sensation of slight distension. If the fistula is connected with the rectum, the internal opening is closed with the finger during the injection, in order that the paste may not penetrate into the rectum, but is forced to follow the course of the fistulous passages. It will occasionally be necessary to effect the injection through the internal opening with the help of a rectoscope. The injection should be repeated if, after a week, purulent secretion is still present; in the presence of serous secretion the fistula soon closes and in this case the injection should not be repeated.

MacKelvey Bell agrees that bismuth paste diminishes pain in acute suppuration, but he has not observed any acceleration in the process of healing; indeed, in non-suppurative wounds he found healing to be delayed and the disease to pass into a chronic condition. The drug has, however, proved reliable in the drainage of abdominal wound cavities.

Even though all authors who have studied the question of the utility of bismuth paste are agreed that the preparation possesses valuable therapeutic properties, the fact must not be overlooked that the use of the paste not uncommonly produces toxic symptoms. Many authors have reported upon

this fact in the past year, such as, S. Erdheim, Laméris, F. Zollinger, W. Peters, L. W. Ely, M. Brandes, Blanchard, R. Hift, M. Sgalitzer and L. Mayer and G. Baehr.

Besides milder and more severe transient cases of poisoning, the authors also observed fatal cases. On the appearance of toxic symptoms, Zollinger recommends irrigation of the fistulous passages with warm olive oil, and if necessary, the splitting up and scraping out of the fistula; and for the treatment of methæmoglobinuria, inhalation of oxygen and saline infusions. Sgalitzer, on the other hand, recommends a careful determination of indications. In his experience, and according to the records in the literature, bismuth injections should be avoided in the pleural and peritoneal cavities, and in joints and abscesses, on account of the danger of poisoning. It should only be used exceptionally and as an ultima ratio in old empyemas, in fistulous articular processes and abscesses, provided the patient agrees to submit to an injection, after having been made acquainted with the dangers of the treatment. 30 c.c. of the 10 p. c. bismuth paste should be considered the maximum dose. But in closed abscesses and in practice among children, Beck's method should under no circumstances be employed.

Beck's method may, on the other hand, be considered free from danger, bearing in mind the maximum dose and employing the correct technique (not too great pressure), in old tuberculous bone disease and in fistulas of the soft parts, which do not lead into an abscess cavity nor into a serous cavity, except in patients having processes leading into the axillæ.

Erdheim, Wiener klinische Wochenschrift 1912, No. 20, p. 749.

Laméris, Nederlandsch Tijdschrift voor Geneeskunde 1912, p. 552.

Zollinger, Bruns, Beiträge zur klinischen Chirurgie 1912, Vol. 77, p. 268.

Peters, Wiener klinische Rundschau 1912, No. 17, p. 257.

Ely, Semaine médicale 1912, No. 28, p. 330.

Brandes, Münchener medizinische Wochenschrift 1912, No. 29, p. 1598, No. 44, p. 2392.

Blanchard, New York Medical Record 1912, No. 20.

Hift, Zentralblatt für die gesamte innere Medizin 1912, Vol. 3, No. 5, p. 211.

Sgalitzer, Wiener klinische Wochenschrift 1912, No. 20, p. 740.

Mayer-Baehr, Surgery, Gynecology and Obstetrics (Chicago) 1912, September, p. 309.

or the groins. Children may also be treated under these conditions, provided the smallest possible amount of the 10 p. c. paste is used for short, straight fistulas. By observing these precautions, Sgalitzer has experienced no instance of poisoning among 80 cases. His results, although not so striking as those reported by Beck, are nevertheless noteworthy, as they would certainly not have been obtained in so short a time by the use of other remedies\*).

Some authors suggest other drugs, alleged to be harmless, in place of bismuth subnitrate. J. R. Mitchell, for curative and diagnostic purposes, used a mixture of powdered chalk and vaseline, and in a case of multiple, tuberculous abscess formation, brought about the closing of the abscess in the course of three months. Blanchard, for the treatment of fistulas, successfully used a paste consisting of 1 part of wax, 8 parts of vaseline and 2 grammes of potassium iodide; and for X ray examinations, he used a mixture of 1 part of sub-carbonate of iron and 2 parts of vaseline. For cold abscesses he prescribed a mixture of 3 parts of wax, 2 parts of paraffin and 24 parts of vaseline. Brandes is of opinion that no preparation has as yet been discovered which is free from the danger of poisoning and at the same time useful for diagnostic and curative purposes. His experiments extend to the employment of zirconium dioxide\*\*), which may prove useful for diagnostic purposes, and to novioiodine, which may be of therapeutic use.

Fath reports a case of anal fissure. The patient was given warm sitz-baths and then placed in the knee-elbow position; by forcible bearing down the fissures were brought into view and were sprinkled with bismuth subnitrate. This procedure was repeated twice daily. The pains disappeared immediately and skin formed over the fissures within a fortnight.

Mention may be made of an ointment containing bismuth which E. Wurm recommends as a protection for the healthy

\*) With regard to the technique of Beck's method of injection, reference should be made to the communications of M. Jerusalem.

— Compare Wiener klinische Rundschau 1912, No. 47, p. 737.  
Mitchell, Journal of the American Medical Association July 29, 1911.

\*\*) Compare Merck's Report 1909, p. 346.

Fath, Münchener medizinische Wochenschrift 1912, No. 35, p. 1934.  
Wurm, Münchener medizinische Wochenschrift 1912, No. 10, p. 532.

skin during the application of X rays. It consists of a glycerin-starch paste containing finely divided lead nitrate and bismuth nitrate. According to the author, it is practically impenetrable to X rays and, after use, can readily be washed away with water.

### Borax.

The numerous recommendations of borax for the treatment of epilepsy\*) induced P. Jödicke to try it in his sanatorium. Before commencing the cure, the patients were carefully examined and only those with healthy excretory organs were chosen. These were given daily doses of 0.9 grammes (14 grains), increasing up to 2 grammes (30 grains), after meals. Only 14 p. c. of the patients treated showed a definite improvement of the epileptic trouble. The author therefore considers the value of borax open to question, but thinks that the lack of interest displayed with regard to borax treatment in Germany to be justified. The secondary symptoms to which the drug gives rise are out of proportion to its utility. One of his patients was obliged to give up the use of the drug after 2 months' treatment, as he suffered from loss of appetite and physical weakness. A. Devaux also considers the secondary effects a sufficient reason for desisting from administering borax, even though he obtained good results in 3 cases. In 2 cases the fits disappeared completely, and in a third case, that of an idiot, the intelligence was even said to have been improved. The author's advice is that resort should only be had to borax therapy in exceptional cases.

### Bromolecithin.

The great success which has attended the use of lecithin in a variety of diseases of the nervous system\*\*), prompted the manufacture of a preparation in which the sedative action of bromine was combined with the tonic action of lecithin. This is bromolecithin, an additive product of bromine and lecithin, containing 25 p. c. of bromine. It is issued in the form of tablets containing 0.05 grammes ( $\frac{3}{4}$  grain).

\*) Compare Merck's Reports 1904 and 1908.

Jödicke, Medizinische Klinik 1912, No. 52, p. 2020.

Devaux, Thèse de Toulouse 1912.

\*\*) Compare this Report p. 1.

Bergell and Braunstein, in carrying out comparative tests with bromolecithin and lecithin, found that bromolecithin was more slowly and less completely dissolved by the body-ferments, and was in part absorbed without decomposition. In anaemia it brings about an increase in the red blood corpuscles and the haemoglobin content, in the same way as lecithin. It is specially useful in nervous insomnia, for which E. Baron used it with benefit. The author also obtained very satisfactory results in migraine, and even in the treatment of the nervous symptoms of Graves's disease. Baron also confirms for bromolecithin the action demonstrated by Danilewski for lecithin, viz., an increase in the energy of the systolic contraction of the heart. In his experience, it is also useful in tabes on account of its sedative action, as well as in neurasthenia with pollutions, vertigo and sexual exhaustion. It is given in daily doses of 5 to 10 tablets.

### Bromural.

According to Takeda's investigations, the narcotic action of bromural is due to the unaltered preparation and not to the liberation of bromine in the organism. In the brain of rabbits, after bromural administration, he found a considerably higher percentage of bromine compounds soluble in ether than of inorganic bromides. In the liver the reverse was the case. Emulsion of brain caused little change in bromural, while liver emulsion decomposed bromural in the space of 3 hours (up to 90 p. c.).

In psycho-neurotic conditions of excitement, especially in lunacy practice, Regensburg used bromural with very satisfactory results. Katschkatschew also recommends it, especially in the hallucinations and phobias of alcoholics, and for the treatment of the insomnia of neurasthenic prisoners. On account of its harmlessness he prescribes it for children, as other authors have done\*). Thus, Schäfer obtained a sat-

Bergell-Braunstein, Therapie der Gegenwart 1905, No. 4, p. 156.

— Merck's Report 1905, p. 124.

Baron, Österreichische Ärztezeitung 1912, No. 10, p. 164.

Takeda, Archives internationales de pharmacodynamie et de thérapie 1911, No. 21, p. 203.

Regensburg, Zentralblatt für die gesamte Therapie 1911, No. 12.

Katschkatschew, Praktitscheskij Wratsch 1912, No. 28.

\*) Merck's Report 1910.

Schäfer, Therapie der Gegenwart 1912, No. 3, p. 143.

isfactory result in a case of hysterical anorexia in a boy aged 4, who could never eat more than a few mouthfuls without vomiting; he gave 1 bromural tablet before each meal for a period of 3 months. The remedy proved equally successful in 3 other cases. To excitable children, who had trouble in falling asleep at night, he gave 1 to 2 tablets in the evening, and thus brought about quiet sleep.

Bromural also displayed a remarkable action in epilepsy. Though the fits were not abolished, yet they occurred more rarely and in a milder form following the use of 3 bromural tablets a day. The nervous twitchings of a 10-year-old boy were completely suppressed by 3 daily doses of 0.3 grammie (5 grains) of bromural. Bromural also proved useful in the night terror of children and in nocturnal enuresis, though in the case of the latter the author attributes the success to the influence of suggestion.

As I have mentioned before, bromural has proved useful in dentistry. Williger gave it especially to excitable children, and found that they tolerated the prick of the needle in inducing local anaesthesia and also the operative procedure without much resistance. One tablet (0.3 grammie) (5 grains) sufficed for children up to 12 years of age; for older children and for adults two tablets were required.

Hoffmann found the induction of anaesthesia by ethyl bromide to be facilitated by the previous administration of a tablet of bromural. In operations which were conducted without anaesthesia, bromural proved such a good sedative that the patients' sensation of fear entirely disappeared. The effect is equally welcome to the dentist and the patient.

Bromural is useful as a sedative in nervous disturbances and attacks of pain. Mattik gave 3 daily doses of 0.3 grammie (5 grains) in troubles of the climacteric, headache, nervous vomiting and insomnia of anaemic individuals, in chorea and nervous palpitation. In a case of inflammation of the ovary with cardiac spasm, constant dreams, insomnia and respiratory trouble, these symptoms disappeared after the daily administration of 3 tablets for a week. A woman, who had for a long time become accustomed to injections of morphine for a

Williger, Deutsche zahnärztliche Zeitung 1912, No. 12.

Hoffmann, Deutsche zahnärztliche Wochenschrift 1912, No. 27, p. 33.

Mattik, Deutsche Medizinalzeitung 1912, No. 18, p. 327.

painful disease and who no longer responded to an increased dose, was enabled to sleep again after taking 2 to 4 bromural tablets during the day, and it was possible to reduce the morphine injections. Bromural is of special value as a soporific for old people and children. Schröder even prescribed it for a woman aged 82 who, in consequence of a slight stroke, was suffering from irregular action of the heart, insomnia and oppression, and had remained unaffected by digitalis. One tablet always brought about quiet sleep.

Reinsch relates his experiences with bromural in seasickness. In several cases he found that a daily dose of 2 to 4 tablets sufficed to get rid of even obstinate symptoms, without giving rise to unpleasant secondary effects. Even though the preparation cannot be considered an actual cure for sea-sickness, it is, in his opinion, suited to render the troubles more bearable, although it does not always remove them completely.

### Caffeine.

In experiments on animals, J. Pal found that caffeine, when injected intravenously, stimulates certain peripheral branches of the sympathetic and is thus capable of dilating the bronchi and of relieving existing bronchial spasm. Thus a new indication is offered for the administration of caffeine. Suitable experiments are required to show in how far the author's results will prove useful in therapeutics.

The pharmacological work carried out by T. Sollmann and Pilcher on the action of caffeine on cardiac activity and circulation can only be referred to here.

Caffeine-Sodium salicylate is, according to von den Velden, of excellent service for vascular paralysis of toxic or bacteriotoxic origin; it is administered subcutaneously for this purpose in doses of 1 c.c. of a 20 p. c. aqueous solution every 2 hours. Not much is to be expected from the internal administration of the drug. As these large doses of caffeine

Schröder, Allgemeine medizinische Zentralzeitung 1912, No. 25, p. 318.

Reinsch, Zentralblatt für die gesamte Therapie 1912, No. 7, p. 337.  
Pal, Deutsche medizinische Wochenschrift 1912, No. 1 and 38.

Sollmann-Pilcher, Journal of Pharmacology and Experimental Therapeutics 1912, p. 19 and 609.

Velden, Therapeutische Monatshefte 1912, No. 1.

often lead to conditions of excitement and insomnia, the medication must be discontinued during the night. The daily dose then consists of 1 to 1.5 grammes (15 to 24 grains).

L. Weile has obtained good results in a series of cases of myocarditis, arterio-sclerosis and cardiac neuroses by using a combination of caffeine and extract of ergot, so-called "ergotin-caffeine" or "myocardol". The preparation is on the market in the form of ampoules and tablets, containing 0.15 gramme ( $2\frac{1}{3}$  grains) of caffeine citrate and 0.85 gramme (13 grains) of ergotin for a dose. It can thus be used internally or subcutaneously, or both methods employed simultaneously. The action after internal administration is the same as following subcutaneous injection, but it takes place rather more slowly. Subcutaneous injection can only be employed when it is possible to sterilise thoroughly the syringe and the site of injection; if in spite of this cutaneous irritation should occur, the injections are discontinued and the drug is administered internally in the form of tablets. At first the contents of half an ampoule are injected every second day, and this is increased to one ampoule, alternating with the internal administration of 3 to 4 tablets, as 4 tablets correspond to 1 ampoule. When 5 to 6 ampoules have been used, the internal administration of ergotin-caffeine is continued. Or internal administration may be employed from the commencement, a daily dose of 3 to 4 tablets being prescribed daily for a week, every second day during the second week, every third day during the third week, and so forth.

### Calcium Chloride and Other Calcium Salts.

On the strength of the interpretation of asthma as a secretory neurosis or an urticaria of the bronchial mucous membrane, and in view of the successful results obtained by E. Meyer and Curschmann in tetany and by Januschke, Chiari and Wright in hay-fever and urticaria by the use

Weile, Münchener medizinische Wochenschrift 1912, No. 19, p. 1044 and No. 28, p. 1555.

Meyer, Therapeutische Monatshefte 1911, No. 7, p. 411. — Merck's Report 1911, p. 184.

Curschmann, Deutsche Zeitschrift für Nervenheilkunde Vol. 39, No. 1 and 2.

Januschke and Chiari, Archiv für experimentelle Pathologie 1911, Vol. 65, p. 120. — Merck's Report 1911, p. 183.

Wright, Lancet 1896.

of calcium salts, Kayser has investigated the use of calcium salts in bronchial asthma. The action of calcium salts, as has been demonstrated in experiments on animals, is shown by a diminution in the excitability of the nervous system, so that the cures observed by Kayser could probably be brought into agreement with this action. The author prescribed:

Rp. Calc. chlorid.	20·0	grammes	( $\frac{2}{3}$ oz)
Syrup.	40·0	"	( $1\frac{1}{3}$ oz)
Aq. destill.	ad	400·0	"

M. Sig.: 1 tablespoonful to be taken in milk every 2 hours.

This medication proved beneficial in 13 cases of typical bronchial asthma and other asthmatic conditions, and also in a case of hay-fever, in which the attacks ceased after 3 to 4 days, and did not recur for many months. The patients asserted that after taking the medicine they were able to breathe more freely, that the phlegm became looser and their night's rest remained undisturbed, until finally the condition of freedom from attacks became continuous. The action almost always became manifest from the third day onwards. It is well to continue the administration of calcium for about a week, during which period the calcium chloride mixture should be taken regularly. As the medication gave rise to no injurious secondary effects, further tests of this method of treatment may be recommended in all cases of bronchial asthma and allied conditions, if apart from emphysema and bronchitis, no other complications are present.

R. Hoffmann, who had previously tried the use of calcium salts for hay-fever, obtained less favourable results. He assumes that his dosage was too low, and that the calcium lactate, which he prescribed with the calcium chloride, was less efficacious than the latter. He administered a daily dose of only 3 tablespoonfuls of a solution of 5 grammes ( $75\frac{1}{2}$  grains) of calcium chloride in 200 grammes ( $6\frac{2}{3}$  oz) of water. Calcium chloride should also be tried, according to the author, in mucous colitis, so closely related to bronchial asthma, in Graves's disease, osteomalacia and otosclerosis. For hay-fever he recommends the following medication, to be begun a week before the expected flowering time of grasses:

Kayser, Therapeutische Monatshefte 1912, No. 3, p. 167.

Hoffmann, Münchener medizinische Wochenschrift 1912, No. 21, p. 1152.

## Rp. Calc. chlorid.

Calc. lact.	aa	10·0 grammes	( $\frac{1}{3}$ oz)
Syrup.		40·0	„ ( $1\frac{1}{3}$ oz)
Aq. destill.		400·0	„ ( $13\frac{1}{3}$ oz)

M. Sig.: 1 tablespoonful to be taken 3 times a day.

On the appearance of the symptoms of the illness, the mixture is given every two hours until a total amount of 40 to 50 grammes ( $1\frac{1}{3}$  to  $1\frac{2}{3}$  oz) of calcium salts has been taken. In another communication, Hoffmann suggested the following prescription, which does not differ essentially from the preceding one:

## Rp. Calc. chlorid.

Calc. lact.	aa	15·0 grammes	( $\frac{1}{2}$ oz)
Syrup.		50·0	„ ( $1\frac{2}{3}$ oz)
Aq. destill.	ad	500·0	„ (17 oz)

Of this, 3 tablespoonfuls a day are to be taken as a prophylactic, and double the amount when the disease has commenced, until 2 bottles have been taken.

Cassidy tried calcium chloride in 50 cases of diphtheria in children, without obtaining satisfactory results; while Wright, after having injected diphtheria antitoxin in a case of urticaria, obtained a satisfactory effect from calcium medication. Possibly the same absorptive action comes into play here as was observed by Courteilmont and Collin in serous exudations. The authors report 2 cases of induration of the pulmonary apices, which were accompanied by fever, vomiting, diarrhoea, emaciation and caseating, tuberculous peritonitis, in which the following medication, together with a dry diet, proved beneficial:

Rp. Calc. carbon.	0·65	gramme	(10 grains)
Calc. phosphor. tribasic.	0·2	„	(3 „ )
Sod. chlorid.	0·15	„	( $2\frac{1}{3}$ „ )

One of these powders is given to the patient morning, noon and night, after meals. Boissoneau was able to confirm

Hoffmann, Therapeutische Monatshefte 1912, No. 5, p. 352. — (Compare also Deutsche medizinische Wochenschrift 1911, No. 20, p. 929.)

Cassidy, Lancet 1911, II., p. 1695.

Courteilmont - Collin, Klinisch - therapeutische Wochenschrift 1912, No. 14, p. 428.

Boissoneau, Klinisch - therapeutische Wochenschrift 1912, No. 39, p. 1152.

the excellent action of calcium chloride in promoting absorption. In numerous cases of pleurisy, ascites, cardiac and renal œdema, the diuretic and tonic action of the drug was manifest. It is prescribed thus:

Rp. Calc. chlorid. 0·3—2·0 grammes (5—30 grains)

Syrup. aurant. flor. 30·0 „ (1 oz)

Aq. destill. ad 150·0 „ (5 oz)

M. Sig.: 1 tablespoonful to be taken every 2 hours.

Calcium salts have in recent years been much used to increase the coagulability of the blood. P. de Vries gave to women, who had suffered from prolonged haemorrhage at previous confinements, 2 grammes (30 grains) of calcium lactate twice a day, about 1 to 2 months before the date of the expected confinement, as a prophylactic measure, and his results were good in every case. But N. Voorhoeve doubts the possibility of increasing the coagulability of the blood in all cases by the administration of calcium, because other factors besides calcium play a part in blood coagulation. For, in the absence of pro-ferment and fibrinogen, for example, it is impossible to cause the coagulation of blood in vitro, however much blood-calcium may be present. It must further be taken into consideration that post-partum haemorrhage is often due to a local cause, in which case the coagulating capacity of the blood in toto would be without effect in arresting the haemorrhage. But the author does not deny that the calcium content of the blood can be increased by the administration of calcium salts, though large doses will certainly be required. He has himself given 15 grammes ( $\frac{1}{2}$  oz) a day of calcium lactate, as after doses of 3 grammes (45 grains) he was unable to demonstrate an increase in the calcium content of the blood. The investigations of J. Parisot and Heully are also in favour of the anti-hæmolytic action of calcium salts. They found that although the commencement of hæmolysis was not delayed, its course was protracted. This effect, however, cannot be confirmed in every case. Thus, in 4 cases of nephritis, the author only twice observed a delay in hæmolysis as a consequence of calcium medication.

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de Vries, Nederlandsch Tijdschrift voor Geneeskunde 1912, No. 55,  
p. 1748.

Voorhoeve, Berliner klinische Wochenschrift 1912, No. 36, p. 1714.

Parisot-Heully, Comptes rendus de la société de biologie 1912,  
Vol. 72, p. 39.

If an increase in the calcium content of the blood is not effected by the internal administration of calcium salts, so that the desired action does not occur, it is best to give injections of calcium chloride gelatin (kalzine), which can be injected without giving rise to local symptoms of irritation. Compare the article on Sterilized Gelatin.

Jakoby and Schroth tried internal calcium medication in a case of osteitis fibrosa, and obtained a good result by the daily administration of up to 10 grammes ( $\frac{1}{3}$  oz) of calcium lactate. An existing fracture of the upper arm was consolidated, and a part of the bone which had undergone cystic degeneration became hard. An investigation of the metabolic processes showed a retention of calcium and a decrease in the abnormal excretion of calcium from the kidneys.

A short time ago A. Zahn described a process for increasing the number of tubercle bacilli in the sputum, blood, exudates and stools, thus facilitating their demonstration. The method consists in adding to the fluid in question first normal caustic soda and then normal calcium chloride, and the bacilli are thrown down in the precipitate. After centrifuging, the precipitate is transferred to a slide and stained in the usual way with carbol-fuchsin and methylene blue. The calcium is removed during the process of decolorisation by alcohol-hydrochloric acid. The author has recently improved the method by the addition of antiformin. For details of the method, reference should be made to the author's original communication.

### Calcium Oxide and Peroxide.

A short time ago L. de Jager described a test for glucose in the urine, which may be regarded as a modification of the well known Trommer's test. In carrying out the test, 20 p. c. milk of lime, prepared from calcium oxide, is used in place of caustic soda or potash. 5 c. c. of the urine to be tested are added to 10 drops of this milk of

Jacoby-Schroth, Mitteilungen aus den Grenzgebieten der Medizin und Chirurgie 1912, Vol. 25, p. 383.

Zahn, Münchener medizinische Wochenschrift 1910, No. 16, p. 840 and 1912, No. 30, p. 1653.

de Jager, Zentralblatt für die gesamte Physiologie und Pathologie des Stoffwechsels 1911, No. 15 and 17. — Zentralblatt für innere Medizin 1912, No. 25, p. 625.

lime and after the addition of 5 drops of a 10 p. c. solution of copper sulphate, the mixture is heated just to boiling. If the mixture is now put on one side, the precipitate which forms will be coloured red to violet in the presence of a small amount of glucose. If the urine contains a greater amount of glucose, instead of this coloration, a precipitate of cuprous oxide will be thrown down. It is stated that by means of this reaction 0·1 p. c. of glucose can be demonstrated. If it is desired to keep the milk of lime required for this reaction in stock, it is better, according to more recent communications by the author, to prepare it from calcium hydroxide, because that prepared from calcium oxide easily becomes too thick, and cannot so well be poured or dropped from the bottle. For this purpose, sufficient water is poured on to 30 grammes of calcium hydroxide to make the mixture up to 100 c. c.; this is left to stand in a well stoppered jar for at least 24 hours before being used, and is shaken at intervals. A bottle with a cork stopper should be used, as a glass stopper would soon become so tightly fixed that it cannot be removed. The test described above is carried out with 5 c. c. of urine, 10 drops of milk of lime and 5 drops of copper sulphate solution. The milk of lime should be well shaken before use.

A further use for lime, according to P. Bergell, is in the analysis of urine for nitrogen. As the estimation of nitrogen is of great interest in the investigation of metabolism, special reference will be made to the author's communications. By the help of his method the wearisome estimation of nitrogen according to Kjeldahl's method can be circumvented, and an accurate result can be obtained in about 12 minutes. For this purpose, 2 c. c. of urine and a few grammes of pure calcium oxide are placed in a quartz test-tube, which is connected in a suitable manner by means of rubber stoppers and glass tubing with a receiver containing 20 c. c. of  $\frac{1}{10}$  normal hydrochloric acid and a little rosolic acid (indicator); the water of the urine-lime mixture is evaporated over an open flame, and the mixture is then gradually heated to redness. The acid in the receiver, which has not been neutralized, is titrated with  $\frac{1}{10}$  normal caustic soda; this gives the amount of hydrochloric acid which has been combined, and from it the amount of nitrogen can be calculated.

**Camphor.**

The value of large doses of camphor in pneumonia is still a matter for careful therapeutic investigation\*). It has been discussed in the past year by A. Seibert, J. Iversen and E. Roser. Seibert, who has for years been in favour of large doses in pneumococcus pneumonia, has sought to support his method by means of pharmacological investigations. He succeeded in that he was able either to cure or to postpone the death of rabbits, which had been fatally infected by pneumococci, by the use of subcutaneous injections of camphor. In human medicine, he prescribes a 30 p. c. camphor oil, of which he injects 10 c. c. for every 50 kilogrammes of body-weight into the outer side of the thigh, every 12 hours in ordinary cases, and every 8 hours in severe cases. The pulmonary symptoms disappeared after the usual time; respiration, temperature and pulse returned to normal after 3 to 4 days, and in no case did injurious secondary effects occur. (Injections of oil of camphor with the addition of salicylic acid are said to be of value in rheumatism.) Iversen also gave 10 to 12 c. c. of oil of camphor (20 p. c.) twice a day, with excellent results. His observations with regard to the disappearance of symptoms are practically identical with those of Seibert. On the strength of equally favourable experiences, Roser also recommends large doses of oil of camphor, which are said to be highly efficacious in croupous pneumonia and the circulatory disturbances accompanying it\*\*). According to A. Swojechotow, internal camphor medication is also useful in pneumonia. He prescribes 0·12 grammes (2 grains) every 2 hours, which does not usually give rise to gastric disturbances. After the occurrence of the crisis, he continues the dose of camphor for several days, at first every 3 hours and later every 4 hours. If this medication does not reduce the pulse rate to or below 120 per minute, he also adopts subcutaneous application of camphor. It is indeed useful in circulatory disturbances in general, as is shown in the communications of v. d. Velden.

\*) Compare Merck's Reports 1909—1911.

Seibert, Medical Record 1912, Vol. 81, p. 750.

Iversen, Russky Vratch 1912, No. 2, p. 46.

Roser, Dissertation Bonn 1912.

\*\*) Compare Merck's Reports 1909, p. 155.

Swojechotow, Semaine médicale 1912, No. 19, p. 222. — Wratschewnaja Gazeta 1912, No. 6.

Besides caffeine\*), the author administered 1 c. c. of strong oil of camphor every hour, especially at night, when caffeine is not indicated. An hourly repetition of the injection is requisite, as its action passes off in this period. He does not advise large single doses (10 to 20 c. c.), such as have been recommended by others. The only disadvantage of this treatment is the formation of small oil abscesses.

Esser and Siegert discuss the dangers attending large doses of camphor. According to Esser, experience teaches that 1 gramme of camphor a day pro 10 kg. of body-weight may be given without ill effects. He himself has frequently exceeded this dose, for example, he has given 10 to 12 grammes a day to a man weighing 70 kg., and 87 grammes of camphor in the space of 10 days to a man weighing 66 kg. (in a case of severe pneumonia affecting several lobes). As a general rule, he injects 5 to 12 syringefuls of oleum camphoratum forte (Ph. G. V. corresponding to lin. camphor. B. P.) at intervals of 8 hours. This medication is particularly beneficial in croupous pneumonia, for it has a stimulating action on the heart and counteracts the depressant effect of toxins; it stimulates the motor apparatus, raises the blood pressure, dilates the vessels of the lesser circulation, thus permitting a better flow of blood through the lungs and occasioning a diminution in pathological resistance; and it acts injuriously upon pneumococci. Siegert confirms Esser's statements. In his experience, no ill effect is ever observed, even on giving 4 grammes of oil of camphor (10 p. c.) pro kg. of body-weight to a baby weighing 4 kg. In older children doses up to 10 grammes of camphor oil give excellent results, even if nephritis is present as a sequen'ce to diphtheria and scarlet fever. Camphor may therefore be considered the stimulant of choice in pediatrics.

The intraperitoneal application of large doses of camphor oil, which has been recommended by various authors\*\*), is not apparently so harmless as has been assumed. According

\*) Compare E. Liebmann, Archiv für experimentelle Pathologie 1912, Vol. 68, p. 59.

Therapeutische Monatshefte 1912, No. 1, p. 1.

Esser-Siegert, Deutsche medizinische Wochenschrift 1912, No. 48, p. 2291.

\*\*) Compare Merck's Reports 1910 and 1911.

to the explanations of Höhne and Happich and the communications of Hirschel and Rübsamen, camphor should be used with circumspection, and with special care in weakly individuals, even though it has been used hitherto with marked success and without lasting harm. This subject has been fully discussed by Rübsamen. He came to the conclusion that for intraperitoneal employment the doses should not be excessive and the concentration of the oil of camphor used should not exceed 1 p. c.; this view is supported by Hirschel and Höhne. In this case, even if 100 to 200 grammes ( $3\frac{1}{3}$ — $6\frac{2}{3}$  oz) are used, there is no danger of giving a fatal dose. Thus it is not necessary to discard a drug which, in the opinion of these authors, is capable of much good. This finds further confirmation in the communications of Vignard and Arnaud.

Lampe considers a 2 p. c. oil of camphor an excellent drug for the treatment of operation wounds. It is poured or rubbed on to the wound itself and the surrounding area, whereupon the rubefacient and chemotactic properties of camphor come into play.

### Carbonic Acid.

During the last few years increasing interest has been shown in dermatological practice for solid carbonic acid or carbonic acid snow pressed into moulds. The only barrier to its general adoption in medical practice is the instability of the preparation. Solid carbonic acid evaporates in a comparatively short time, so that it is impossible to keep in stock the little pencils of carbonic acid required in practice, or to manufacture them for export. Requests of this nature cannot therefore be complied with. Treatment with carbonic acid snow is therefore at present restricted to hospitals and to skin specialists, who have always access to solid carbonic acid and can keep the liquid carbonic acid, required for its preparation, ready for use in steel receivers. I cannot enter here

Höhne, Münchener medizinische Wochenschrift 1912, No. 16, p. 871.  
Happich, Münchener medizinische Wochenschrift 1912, No. 12, p. 641,  
No. 23, p. 1273.

Hirschel, Münchener medizinische Wochenschrift 1912, No. 37,  
p. 2004.

Rübsamen, Zentralblatt für Gynäkologie 1912, No. 31, p. 1009.

Vignard-Arnaud, Revue de chirurgie 1912, No. 5.

Lampe, Medizinische Klinik 1912, No. 17, p. 711.

into the details of preparation, as reference can easily be made to text-books of physics\*). For the compression of carbonic acid snow special apparatus is, of course, required, by means of which the carbonic acid pencils can be prepared shortly before use. H. L. Heusner has described the apparatus and the method of obtaining the solid form from liquid carbonic acid.

F. Rössler tried cauterisation by carbonic acid, according to Harston's process, in a few cases of trachoma, but did not obtain equally good results. In order to come to a satisfactory decision as to which treatment was best, viz., the usual treatment with silver nitrate or cauterisation with carbonic acid, the author only selected those patients who had both eyes equally affected. The one eye was treated with silver nitrate, the other with carbonic acid. This showed that treatment by carbonic acid afforded no advantages. Healing does not take place more quickly, the trachoma granules yield slowly as compared with the older method and there is greater scar formation. In the presence of granules on the scleral conjunctiva, treatment by carbonic acid is a complete failure. Pannus formation, in the author's experience, remains uninfluenced.

J. Capauner suggests a method of treatment of cavernomata of the lids. It also depends upon cauterisation with carbonic acid pencils, and gives rise to a more or less strong reaction, lasting in proportion to the duration of its application from 5 to 60 seconds. The oftener the treatment is repeated, the weaker does the reaction become. If the application of carbonic acid to the lids is prolonged, a plate should be inserted for the protection of the cornea. An action of 5 to 10 seconds causes dermatitis without the formation of scurf, which heals in about 5 days; an action of 10 seconds gives rise, in the course of a few hours, to a swelling like that caused by the bite of an insect, and on the third day to a crust which heals in 10 days without scar formation; an action of 20 to 30 seconds gives rise to a blister in about 6 to 8 hours, which heals in 10 to 20 days, sometimes with

\*) Compare Müller-Pouillet's, *Lehrbuch der Physik* 1907, III, p. 418.  
Heusner, *Deutsche medizinische Wochenschrift* 1912, No. 47, p. 2220.

Rössler, *Wiener klinische Wochenschrift* 1912, No. 2, p. 87.

Harston, *Merck's Report* 1911, p. 190.

Capauner, *Klinische Monatsblätter für Augenheilkunde* 1911, Vol. 12, p. 641.

slight scar formation. An action of 50 to 60 seconds causes an adherent scurf and a smooth, white scar. It is best, according to the author, to begin with a brief period of action and to increase it gradually. The author does not discuss the results of this treatment.

A new method of applying carbonic acid, of which further tests are required, is that suggested by Graeme Anderson for haemorrhoids. The author had the patient anaesthetised with ether, the sphincter ani stretched and solid carbonic acid applied to the piles for about 20 seconds. He states that in the successful cases the piles showed inflammatory symptoms, infiltrations and granulations of the connective tissue.

By its rapidity of action, freedom from danger and good cosmetic results, carbonic acid treatment is excellent, according to the communications of J. Meneau, Nystroem, A. Halle and L. E. Merian, for angiomatous, verrucous and pigmented naevi, lupus erythematosus, greatly depressed scars of pocks and acne, keloids, superficial epitheliomata, hyperkeratosis, etc. In the treatment of cutaneous cancer, the extent of the area treated with carbonic acid plays an important part, as the depth of action increases proportionately. Other noteworthy points in the treatment of the diseases mentioned have been discussed in my earlier Reports.

### Charcoal, Animal

In my Reports for 1909 and 1910 I drew attention to the use of animal charcoal in fungus poisoning. The excellent results obtained by O. Adler in diarrhoea, enteritis and severe cases of poisoning with mineral poisons would justify a more extended use of animal charcoal.

As is shown by Greef's investigations, animal charcoal possesses the advantage of greater absorptive power over other substances, such as kaolin, neutralon and bismuth sub-

Anderson, British Medical Journal 1912, I, p. 120.

Meneau, Gazette des hôpitaux 1911, December.

Nystroem, Deutsche Zeitschrift für Chirurgie 1912, No. 6.

Halle, Archiv für Dermatologie und Syphiligraphie 1912, p. 385.

Merian, Medizinische Klinik 1912, p. 481.

Adler, Wiener klinische Wochenschrift 1912, No. 21, p. 788.

Greef, Dissertation Göttingen 1911. — Münchener medizinische Wochenschrift 1912, No. 26, p. 1458.

nitrate. The good effect of the preparation observed by Adler may be considered to be due to this property. It possesses the property of absorbing the toxins produced by the bacteria, which give rise to severe irritation of the intestinal walls, and of inhibiting the further development of the bacteria themselves. The experiments on this subject, which Adler carried out on a healthy person, showed that the number of bacteria present in the faeces was reduced a hundred fold by the administration of animal charcoal.

The earlier the administration of animal charcoal is commenced in cases of gastro-enteritis and acute enteritis, the more favourable will be the results, as in these cases the injury to the intestinal walls is still slight or absent. In these cases, the administration of 3 daily doses of 3 to 5 grammes (45—75 grains) for several days suffice to effect the disappearance of diarrhoea. But it is advisable to continue the medication for a few more days to prevent recurrences. In typhoid fever, Adler did not obtain a definite improvement, and, as in febrile dysentery, a rise of temperature could not be prevented. On the other hand, two persons suffering from para-typhoid were relieved of fever and other symptoms within 6 and 9 days respectively after animal charcoal medication. In cholera, treatment by animal charcoal also promises success, but further experiences are required. Of course, in cases of intestinal tuberculosis and in enteritis accompanied by changes in the intestinal wall no great benefit can be expected from charcoal therapy.

According to Adler's results, animal charcoal would appear to be indispensable in cases of poisoning. In a case of phosphorus poisoning, in which a large amount of phosphorus had been present in the intestinal tract for 20 hours, animal charcoal was administered (by mouth and rectum); severe vomiting and jaundice ensued, but the patient recovered. In another patient, who came under treatment 3 hours after the ingestion of phosphorus, no toxic symptoms occurred, although a considerable amount of phosphorus had been consumed. Treatment consisted in gastric lavage with permanganate solution, and administration of repeated doses of 5 grammes (75 grains) of animal charcoal, and rectal irrigation with a suspension of 15 grammes ( $\frac{1}{2}$  oz) of animal charcoal in 20 litres (35 pints) of water. In a case of poisoning by 3

corrosive sublimate pastilles, besides the exhibition of milk and fluid egg-albumin, and in addition to gastric and intestinal irrigation, 10 grammes ( $\frac{1}{3}$  oz) of animal charcoal were administered. The patient was discharged cured after 5 days and no further toxic symptoms occurred. Treatment by animal charcoal was equally successful in poisoning by phloroglucin and Schweinfurth green.

As the deep black colour of the charcoal suspension excited strong antipathy against the medicament in isolated cases, Adler added kaolin to the mixture, the powerful absorbant action of which is well known; the medicine was thus improved in appearance, while its efficacy remained as before, or was even increased.

### Chenopodium Oil.

The utility of wormseed oil in the treatment of ascaridiasis, to which H. Brüning drew attention several years ago, has been since confirmed by F. Thelen, W. Schmitz and M. Gockel. As this oil possesses a peculiar, scratchy taste, which makes it unpleasant, especially for children, Brüning has recently recommended a mixture of 1.5 grammes of American wormseed oil and 48.5 grammes of castor oil, to which saccharin and essential oils are added to improve the taste. The preparation is issued under the name of "Wermolin".

Brüning prescribed the preparation in 16 cases in children aged 2 to 14. In no case, according to his communications, did the drug cause trouble. He gave it in small teaspoonfuls night and morning and always found three such doses to suffice. To increase its aperient action, castor oil or compound liquorice powder was given at the same time. By means of this medication, the worms were got rid of in every case, without giving rise to subjective troubles. The author believes that wermolin will prove of value in the form of rectal injections for thread worms, but he has no personal experience on the subject.

Brüning, Merck's Report 1906, p. 179.

Thelen, Dissertation Rostock 1907.

Schmitz, Dissertation Bonn 1908.

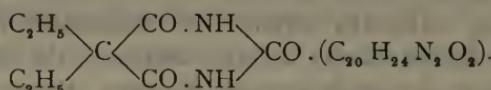
Gockel, Merck's Report 1910, p. 259.

Brüning, Deutsche medizinische Wochenschrift 1912, No. 50, p. 2368.

**Chineonal.**

Chineonal is the quinine salt of diethyl-barbituric acid (veronal), containing 63.78 p. c. of quinine and 36.22 p. c. of veronal. It is a uniform, chemical compound, which forms colourless crystals, melting at 132° C. The preparation dissolves with difficulty in water, more readily in alcohol and chloroform.

Chemical formula:



When clinical experience had shown that the mild narcotic action of quinine could be effectively intensified by veronal, the need was felt for a suitable preparation, which combined in itself the action of quinine and of veronal, and at the same time possessed chemically and pharmacologically stable properties, as well as uniform composition. Chineonal fulfills these requirements. The pharmacological investigation of the drug showed it to be non-irritant both to the stomach and to mucous membranes. Rabbits tolerated doses of 1 gramme, given on several consecutive days, without ill effect. The urine and blood remained normal, and the body-weight showed no decrease. In experiments on dogs, fever brought on experimentally by extract of hay bacilli was reduced without the occurrence of vomiting, which usually follows the administration of quinine.

This experience was confirmed in human medicine. H. Winternitz administered 0.6 to 0.75 gramme (9 to 12 grains) of chineonal several times daily for many days to feverish patients, who were delirious or suffering much pain; as a result of numerous trials, he found that the drug was well tolerated and gave rise to vomiting less often than quinine; and further that the secondary effects, so often occurring after the administration of quinine, either remained absent or occurred in a milder form when chineonal was used.

As might be expected, chineonal is also of service in whooping-cough. H. Fränkel and K. Hauptmann report upon its use. Experiments on 30 children showed that it

Winternitz, Medizinische Klinik 1912, No. 15, p. 614. — Merck's Archives 1912, p. 311.

Fränkel-Hauptmann, Medizinische Klinik 1912, No. 46, p. 1871.

gave a positive result in 26 cases and a negative result in 4 cases. In the successful cases, the attacks of coughing were rapidly reduced in number and severity, vomiting soon ceased and the appetite was usually improved. It was apparent that on the whole the action of chineonal was superior to that of quinine, and that it was better tolerated and more willingly taken than the latter. The fact that the preparation failed in 4 cases is explained by the authors in that the patients were severely ill and in the convulsive stage; such cases are as a rule little influenced by drugs. But among the successful cases, some were also in the convulsive stage, so that a beneficial action is not excluded in these cases. Children in the first year of life were given 0·1 grammie ( $1\frac{1}{2}$  grains) of chineonal 3 times a day, and older children 0·2 grammie (3 grains) 3 times a day. Secondary effects did not occur with this dosage.

According to G. Armbruster, chineonal, which is also of value in some varieties of sore throat and in shivering with insomnia resulting from exposure to damp and cold weather, is capable of preventing the occurrence of whooping-cough altogether. It gives excellent results also in nocturnal attacks.

Chineonal is useful, not only in infective fevers, such as malaria, typhoid, influenza and septic articular rheumatism, but also, on account of its marked narcotic action, as a general nerve sedative, as well as a sedative in neuralgia. It may also prove of value in sea-sickness, for which quinine and veronal have been used with benefit. Its employment may, in fact, be recommended for all cases in which a mild quinine preparation is indicated, which is well tolerated and occasions no harm locally.

Chineonal is administered in doses of 0·6 grammie (9 grains) at noon or in the evening, according to the nature of the case. If it is desired to procure rest for delirious patients suffering from pain, 0·6 grammie (9 grains) are given several times a day. Children are given daily doses of 0·2 grammie (3 grains), and in whooping-cough 0·1 to 0·2 grammie ( $1\frac{1}{2}$  to 3 grains) 3 times a day. As chineonal has a very bitter taste, it is best to use tablets containing 0·3 grammie (5 grains) of chineonal, which are swallowed whole with a little water. The sugar-coated tablets prepared by me, containing 0·1 and

0.2 gramm (1½ and 3 grains) of chineonal are specially suitable for sensitive patients.

### Cholesterin.

J. Pringsheim sought to determine the significance and the value of cholesterin in haemoglobinuria. He carried out experiments on a patient aged 34, who was suffering from haemoglobinuria, and chose intramuscular administration, because the drug was more likely to be completely absorbed into the circulation by this method than by internal administration. As the result of an experiment on a rabbit, the author was convinced that the 10 p. c. aqueous emulsion of cholesterin which he used was rapidly absorbed. The injections of these emulsions in man are moderately painful and occasionally give rise to painful infiltrations, which do not disappear for 2 to 3 weeks. After several injections of the absolutely sterile emulsion, the author observed a slight rise in temperature. But there is no fear of poisoning, even with large doses of cholesterin.

The case reported by the author dealt with a patient who gave a positive Wassermann reaction. He was therefore given an energetic course of treatment by inunction, which was, however, unsuccessful, for walks were regularly followed by a slight rise in temperature and haemoglobinuria. On the other hand, intramuscular injections of 0.5 gramm (7½ grains) of cholesterin a day had a distinct effect. After 5 injections in the course of 11 days, the same degree of cold which had formerly called forth severe attacks, only gave rise to slight haemoglobinuria; and after a further injection, the urine remained altogether free from haemoglobin. The author was unable to decide whether, in order to prevent the occurrence of an attack, it was necessary to enrich the blood with cholesterin, or whether a single supply of cholesterin shortly before the experiment is sufficient.

### Choleval.

It has been known for some time, from the investigations of various observers, that bile possesses to a certain degree bactericidal and bacteriolytic properties. These properties are

plainly evident in some pathogenic bacteria, while with others they are almost, or entirely, absent. Löhlein has made a careful study of the action of bile, or of bile salts, on gonococci; he found that sodium taurocholate, and more so sodium glycocholate, have a markedly destructive action on gonococci. But these salts also possess the property of dissolving secretions, so that the gonococci which cannot be acted upon directly owing to the presence of pus, or of pus cells and epithelial cells, fall a prey to the bactericidal action of the bile salts. Löhlein was also able to demonstrate the high therapeutic value of bile salts in ophthalmia neonatorum. Stimulated by these results, which promise a rapid and radical cure of gonorrhœa, Dufaux has tried the efficacy of bile salts in the treatment of urethral gonorrhœa. On account of their activity in dissolving secretions, of rapidly destroying pus cells and of causing the superficial, loosened epithelial layers to be thrown off, these gonococcus-destroying salts would appear specially suited for this purpose. The only characteristics wanting to make a really efficacious remedy for gonorrhœa are an astringent action, the property of checking secretion and an anti-catarrhal action. Dufaux therefore combined bile salts with colloid silver, a combination which has received the name of "Choleval".

Dufaux's experiments have shown that an effective solution for the treatment of urethral gonorrhœa is that containing 2 p. c. of colloid silver and 7.5 p. c. of sodium choleinate. The author suggests the following method for use in practice. At first a 5 p. c. aqueous solution of choleval is used, which is mixed with double the amount of water and later with an equal amount of water, and this dilution is injected. Finally it is injected undiluted. If no irritative symptoms ensue, more concentrated solutions are gradually used, up to 10 and 15 p. c., and exceptionally even up to 20 p. c. As soon as the purulent discharge has been converted into a slight serous discharge, the medication is not discontinued, but the choleval solution is gradually made more and more dilute. By means of this method of treatment, gonorrhœa is said to be cured more rapidly, more completely and more

Löhlein, Klinische Monatsblätter für Augenheilkunde 1909, Vol. 6  
and 7.

Dufaux, Zeitschrift für Urologie 1912, Vol. 6.

smoothly than by other means. Dufaux has not observed complications during treatment by choleval.

The value of choleval therapy has been fully confirmed in a publication by K. v. Hofmann.

### Choline.

R. Werner reports that there is experimental evidence that basic choline exerts a similar pharmacological action to that of radium irradiation. Schwarz explained this by attributing the biological action of radium rays to the decomposition products of the lipoids, to which they give rise and of which choline is one. For this reason an attempt has been made to utilise choline therapeutically, like radium, in carcinoma and sarcoma. Basic choline, according to Werner, was injected into the tumour in the form of a 10 or 50 p. c. solution; but the results were not satisfactory, as it merely gave rise to severe local necrosis and exerted a comparatively slight action on the surrounding tissue. 2 to 5 p. c. solutions may, on the other hand, be used for intra-tumoral and para-tumoral injections. 0.5 to 1 p. c. solutions were only applied by subcutaneous and intramuscular injection into the thigh. The largest dose used was 2 grammes (30 grains) a day. The author did not exceed this dose, as it caused severe symptoms of poisoning in two persons. The action on tumours was slight when the injections were given at the site chosen; it merely consisted in a slight shrinkage of the tumours. It was better with intra-tumoral and para-tumoral injections, which led either to shrinkage and induration, or to liquefaction of the tumours. But a remnant of tumour cells always remained and was not affected by the dosage mentioned. Thus the author did not achieve a complete success by means of choline treatment. 43 out of 74 patients were temporarily improved, while the remainder were either unaffected or grew worse.

As Werner attributed the failures partly to the readiness with which basic choline is decomposed, and as the efficacy

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Hofmann, Wiener klinische Wochenschrift 1912, No. 44, p. 1742.

Werner, Medizinische Klinik 1912, No. 28, p. 1160. Compare also:

Meidner, Therapie der Gegenwart 1912, No. 8, p. 362 and

No. 10, p. 479; Werner and Szécsi, Medizinische Klinik 1912,

No. 36, p. 1466; Czerny, ibid. No. 36, p. 1467 and Münchener

medizinische Wochenschrift 1912, No. 41, p. 2210.

of choline hydrochloride was shown to be slight, he experimented with the choline salts of weak acids, such as the salts of boric acid, formic acid, amido-acetic acid, iodo-benzoic acid, atoxylic acid and nucleinic acid. The more favourable results obtained by these in sarcomata and carcinomata of mice and rats, induced Werner to experiment with choline borate, iodo-benzoate and atoxylate. The preparations were injected intravenously and subcutaneously at the site chosen, or were given by intra-tumoral or para-tumoral injection. As a rule, the doses did not exceed 25 to 40 c. c. a day of the 2 p. c. solution, and the injections were usually administered 2 to 4 times a week. For injections at the site chosen, dilutions with three or four times the amount of physiological salt solution were used, for injections into veins 10 to 15 fold dilutions. Disturbances of the general health were not observed. Werner considers the direct toxicity of the injections to be so slight that it appears permissible to increase the doses; but in view of the possibility of cumulative action, he has not exceeded them. After 4 to 6 weeks of treatment, the author observed signs of diminution of the tumour, showing choline, especially in combination with mesothorium irradiation, to be a valuable drug. In none of his cases did the author observe any aggravation of the affection. Nevertheless, he does not at present consider it possible to offer an opinion as to the value of his method in human cancer\*).

S t. Szécsi has also carried out pharmacological investigations, and considers a combination of choline and colloid selenium-vanadium to be valuable. He considers the most suitable choline salts to be choline borate and choline iodo-benzoate.

### Chrysarobin.

J. Iggersheimer and P. Cohn discuss so-called "chrysarobin conjunctivitis". Iggersheimer does not consider the designation of this eye disease to be altogether apt, as the

\*) Compare H. Ribbert, *Medizinische Klinik* 1912, No. 49, p. 1983.  
Szécsi, *Medizinische Klinik* 1912, No. 28, p. 1162.

Iggersheimer, *Klinische Monatsblätter für Augenheilkunde* 1912,  
No. 5, p. 518.

Cohn, *Wochenschrift für Therapie und Hygiene des Auges* 1912,  
No. 43, p. 353.

conjunctiva is only inflamed and swollen in the mildest cases, while in the majority of cases the cornea is also severely affected. It will therefore be better in future to use the term "chrysarobin keratitis". Cohn also describes a typical case of keratitis of this kind. The patient had been treated with chrysarobin for psoriasis. The eye-lids were greatly swollen, the conjunctiva inflamed, and the cornea, in the presence of epiphora and marked photophobia, showed distinct epithelial opacity. On discontinuing the administration of chrysarobin, the symptoms of disease immediately improved and a cure followed. If in these cases treatment by chrysarobin is continued, the corneal epithelium becomes detached in the form of little vesicles, groove-like opacities occur and ulcers may even form. Iggersheimer also quotes similar cases observed by Linde, Lewin and Guillery, and refers to the work of Loewenson and Krause on this subject. As in the case reported by Cohn, chrysarobin keratitis usually appears to be due to the careless or unintentional introduction of chrysarobin directly into the eyes. The disease has not, at any rate, been shown to be caused by the absorption of chrysarobin. In one case, however, Iggersheimer assumes that this occurred. Treatment is limited to the discontinuance of the application of chrysarobin and the employment of boric acid.

### Cimicifugin.

Cimicifugin, the active principle of *Cimicifuga racemosa*, is a resinoid of a brown colour, which dissolves almost completely in alcohol. It has hitherto been employed chiefly for nervous symptoms and as an antispasmodic, and has been recommended by Robin and Mendel for aural tinnitus. According to these authors, it has given excellent results in these cases\*).

Linde, Deutsche medizinische Wochenschrift 1898, p. 519.

Lewin-Guillery, Wirkungen von Arzneien und Giftmitteln auf das Auge II., p. 775.

Loewenson, Zeitschrift für Augenheilkunde, Vol. 5, p. 486.

Kraus, Zeitschrift für Augenheilkunde, Vol. 15, p. 233.

Robin-Mendel, Médecine moderne 1898, No. 38.

\*) 0·06 to 0·1 gramme (1 to  $1\frac{1}{2}$  grains) may be regarded as the single dose of cimicifugin. About four times this amount may be given during the day. Compare Merck's Index 1910, p. 82.

As besides other measures for the treatment and cure of subjective noises, drug treatment cannot be left out of account, K. Theimer has recently once more resorted to cimicifugin in the treatment of aural tinnitus, and his results on the whole confirmed those of the above named authors. He combined cimicifugin with two other sedatives, namely bromine and phosphorus, a preparation which is on the market in the form of tablets, under the designation "Otosclerol". At first he administered 3 tablets a day and rapidly increased the daily dose to 15 tablets, which amount was continued for a time. His experiences lead him to expect a cure in many cases of commencing tinnitus, but he has not had sufficient cases to form a definite opinion.

### Cineol.

Cineol,  $C_{10}H_{18}O$ , which is well known as a component of wormseed oil, and is, according to Semmler, identical with eucalyptol and cajeputol\*), was investigated by H. Brüning for possible vermicidal properties. The idea for this examination was supplied by the possibility that cineol might play a part with santonin in the action of wormseed. But experimental investigations on animals and human beings showed that little or nothing was to be expected from cineol in this direction. Round worms, which were kept for a few days in a solution of sodium chloride containing 0.05 p. c. of cineol, were at the end of this time just as lively as others which had been kept in pure water. In children suffering from round worms, the preparation proved a complete failure, and quite small doses gave rise to abdominal pain, nausea and vomiting, so that it may justly be assumed that the drug is without value as an ascaricide.

### Coal Tar.

The use of crude coal tar and its utility in dermatology is enlarged upon in a publication by E. Müller. According to this, the preparation should only be used in skin diseases

Theimer, Österreichische Ärztezeitung 1912, No. 7, p. 111.

Semmler, Die ätherischen Öle, Leipzig 1906.

\*) Compare Merck's Index 1910, p. 101.

Brüning, Zeitschrift für experimentelle Pathologie und Therapie 1912, Vol. 11, No. 1, p. 155.

Müller, Deutsche medizinische Wochenschrift 1912, No. 23, p. 1095.

when the process of healing has already been initiated by the use of other medicaments. The author therefore recommends preliminary treatment by moist dressings, pastes, ointments, ichthyl and tumenol. Attention should be directed to the author's suggestion that the tar should always first be tested on a small area, and that general treatment by tar should only be resorted to if the tar is well tolerated in the experimental area. In this way irritation caused by too early employment of tar can be avoided and hypersensitiveness to the drug can be recognised. Attention should also be directed to the efficacy of the tar, for coal tar is not always of uniform composition. Therefore on procuring the tar, it should first be tested in a suitable case and its efficacy established.

Coal tar is specially indicated, according to Müller, in chronic eczema, in which it is said to be practically indispensable. In almost every case in which it was used it was found to alleviate itching, dry up secretion, effect anaemia of the part, diminish infiltration and stimulate the formation of epithelium. Treatment by tar appeared to effect a cure more rapidly than did the employment of pastes and ointments, and the tar also appeared to be more effectual in preventing relapses.

After the preliminary treatment mentioned above, a thin layer of tar is applied by means of a brush, and when the part has dried (powder being used if necessary) it is dressed with muslin bandages. The tar is removed by means of dressings covered with zinc paste containing ichthyl or with lead-vaseline. The tar is usually allowed to act for 48 hours, and, if necessary, it may be renewed after 24 hours without cleansing.

Although the field of employment of coal tar is limited, only extending to chronic eczema, yet tar is of such excellent use within these limits that on account of the ease with which it may be applied and of its cheapness, it deserves full consideration among the list of useful dermatological remedies.

### Cobalt and Sodium Nitrite.

As a substitute for the costly platinum chloride, sodium and cobalt nitrite, proposed by de Koninck, has for many

de Koninck, Merck's Reagenzien-Verzeichnis 1908, p. 140.

years proved of value as a test for potassium salts. Erdmann has also recommended a solution of the salt and has given a formula for its preparation. This test was sufficiently sensitive for qualitative estimation, for even in 0·01 p. c. potassium solutions it caused a perceptible cloudiness due to the formation of potassium and cobalt nitrite, at any rate after a short time. A modification of this test, by which the sensitiveness is increased, so that dilutions containing 0·0001 p. c. of potassium can be demonstrated, has been suggested by L. Burgess and O. Kamm. According to their instructions, one drop of 25 p. c. cobalt and sodium nitrite solution and a few drops of  $\frac{1}{100}$  normal silver nitrate solution are added to 100 c. c. of the solution to be tested, which must of course be free from heavy metals and ammonium salts. In the presence of a minute amount of potassium, a yellow to orange-yellow precipitate of silver-potassium-cobalt nitrite is immediately formed. This precipitate is not suited for quantitative estimation, as it contains varying amounts of silver, according to the amount of silver nitrate added, and on washing with water, it passes into the colloid form. It also usually contains sodium. Under certain conditions, cobalt and sodium nitrite solution may also be used as a test for other salts. Thus, Erdmann has used the reagent as a test for rubidium. According to Burgess and Kamm, it may be used, in the absence of potassium, as a test for ammonium salts, and for the identification of caesium and thallium, as the compounds of caesium and thallium, which correspond to silver-potassium-cobalt nitrite, are even less soluble than the latter.

Bowser gave the following directions for the preparation of the reagent: 220 grammes of sodium nitrite are dissolved in 400 c. c. of water, and 113 grammes of cobalt acetate are dissolved in 300 c. c. of water. The two solutions are mixed and 100 c. c. of glacial acetic acid added. By heating and evacuation, the mixture is freed from the nitrogen dioxide which has formed; it is then filtered and made up to 1 litre with water.

Erdmann, Merck's Reagenzien-Verzeichnis 1908, p. 71.

Burgess-Kamm, Journal of the American Chemical Society 1912,  
Vol. 34, p. 652.

Bowser, Répertoire de pharmacie 1911, p. 545.

### Cocaine Hydrochloride.

When the gastric mucous membrane is in a condition of over-sensitiveness, diarrhoea frequently occurs immediately after meals. This symptom, which is probably a manifestation of reflex action, can, according to E. Fuld, be successfully treated by the use of medicaments which influence the gastric hyper-sensitiveness and the intestinal reflex. For this purpose a solution is used consisting of 0.3 gramm (5 grains) of cocaine hydrochloride and 0.3 gramm (5 grains) of codeine phosphate in 10 grammes ( $\frac{1}{3}$  oz) of peppermint water. 10 drops of this are given to adults before the three chief meals of the day. Children are given as many drops of a solution which is three times weaker as they are years old. In about 50 cases the author found that the diarrhoea was usually checked after a few doses of this mixture, but to avoid recurrences, the drug should be continued for a few days, or even weeks. This can readily be done, as the medicine does not lead to constipation and no special diet is required.

### Codeine Phosphate.

A. Leroy reports upon the value of codeine in psychiatry, especially for the treatment of melancholia. According to him, the alkaloid cannot be looked upon as a reliable medicament, for the subcutaneous administration of 0.05 to 0.1 gramm ( $\frac{3}{4}$  to  $1\frac{1}{2}$  grains) did not cause an improvement in the maniacal conditions, and doses of even 0.15 gramm ( $2\frac{1}{3}$  grains) showed only a variable and uncertain action in the fear and mental distress of melancholia. In a woman who suffered from periodic attacks of mania, the first administration was beneficial, but it failed during the next attack. In two other cases of mania, increasing doses up to 0.6 gramm (9 grains) brought about a condition of calm, but the excitement which followed the discontinuance of the medicament remained uninfluenced.

In conditions of depression codeine is well tolerated, and in only two out of 14 cases did it give rise to lasting nausea. Even the immediate suppression of an attack by means of the enormous dose of 1.6 grammes (25 grains) gave rise to

Fuld, Semaine médicale 1912, No. 35, p. 409.

Leroy, Journal de neurologie 1912, 20<sup>th</sup> May. — Zentralblatt der gesamten Arzneimittelkunde 1912, No. 5, p. 240.

no undesirable effects. The dose of 0·4 gramm (6 grains) was borne without ill effect by a child, who had by mistake taken this large amount internally. But, in the author's experience, there exist sensitive persons in whom vomiting is caused by the administration of 0·02 gramm ( $\frac{1}{3}$  grain) of codeine.

### Codeonal.

Codeonal is a mixture of 11·8 p. c. of codeine diethyl-barbiturate and 88·2 p. c. of sodium diethyl-barbiturate, which is placed on the market in the form of tablets. Each tablet contains 0·17 gramm ( $\frac{2}{3}$  grains) of codeonal (i. e., 0·15 gramm ( $\frac{2}{3}$  grains) of sodium diethyl-barbiturate and 0·02 gramm ( $\frac{1}{3}$  grain) of codeine diethyl-barbiturate). The combination of these two drugs is founded upon the investigations of Bürgi and Homburger, according to which narcotics which are not chemically related, when administered simultaneously or one immediately after the other, show an action which is more powerful than that corresponding to the sum of the actions of the two narcotics.

Pharmacological and clinical tests of codeonal have been carried out by C. Bachem, O. Gaupp, G. Beyerhaus, H. Stursberg, Dornblüth, von Oy, Grzibek and Becker. According to these, codeonal is a useful hypnotic which has the advantage over other hypnotics of not causing a depression of temperature. Bachem has drawn special attention to this fact. Gaupp found that the preparation never acts injuriously on the circulation and only rarely causes secondary effects. Only in a few cases of gastric affections did he observe vomiting and abdominal pain to follow the administration of the drug. The author found that the prolonged use of codeonal did not give rise to a drug habit, nor to constipation, and this was confirmed by Beyerhaus. Accord-

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Bachem, Berliner klinische Wochenschrift 1912, No. 6, p. 260.

Gaupp, Berliner klinische Wochenschrift 1912, No. 7, p. 306.

Beyerhaus, Deutsche medizinische Wochenschrift 1912, No. 9, p. 405.

Stursberg, Münchener medizinische Wochenschrift 1912, No. 18, p. 983.

Dornblüth, Die Schlaflosigkeit, Leipzig 1912.

von Oy, Medizinische Klinik 1912, No. 49, p. 1991.

Grzibek, Psychiatrisch-neurologische Wochenschrift 1912, No. 9.

Becker, Moderne Medizin 1912, No. 10.

ing to Stursberg and Grzibek, 2 to 3 tablets practically always brought about 6 to 7 hours' quiet sleep. Becker also expresses himself well satisfied with the rapid action of the preparation. In mild conditions of excitement and insomnia it is particularly beneficial and its action is comparable to that of 5 grammes (85 min.) of paraldehyde. On the other hand, it usually fails in severe conditions of excitement, in which it cannot replace injections of scopolamine-morphine. According to von Oy, codeonal is specially efficacious in cases in which respiratory troubles predominate, such as bronchitis, pleurisy and tuberculosis, in which the cough is not too severe. Codeonal is also of service as a hypnotic in cardiac disease accompanied by mental distress. It only acts as a sedative in mild cases, such as in cases of slight physical and mental restlessness, and in doses up to 3 tablets in cases of neurasthenia and hysteria. It failed absolutely, according to the author, in the restlessness accompanying senile dementia, in two cases of melancholia, in a case of fantastic paranoia and in a few cases of alcoholic delirium. Von Oy did not exceed a dose of 4 tablets.

### Cod Liver Oil.

In the administration of cod liver oil, individualism cannot be left altogether out of account, however harmless the drug may appear. A. Czerny reports from the Strassburg Children's Hospital that, by the advice of a colleague, in order to obtain better effects, he gave large doses of cod liver oil experimentally at the tuberculosis dispensary. He gave as much as was tolerated without evident disturbance and found that some children were able to take up to 80 grammes (3 oz) a day. But the desired effect was not obtained, for this period of extreme feeding with cod liver oil was not specially evident in the weight curves of the children. On the other hand, one child after the other was affected by eczema of the face and head, and in a few weeks the tuberculosis dispensary had become a scrofula dispensary. On discontinuing the cod liver oil medication, the symptoms disappeared in the course of a few weeks. This observation shows that not only does excess of milk fat have an unfavourable effect on the symptoms of the exudative diathesis of

sucklings, as is well known, but that these symptoms may be provoked in older children by an extremely fatty diet. The author therefore states that when tuberculosis exists in combination with an exudative diathesis, the fat content of the food should be carefully regulated. If the diet is otherwise poor in fat, 2 tablespoonfuls of cod liver oil a day may be given.

### Copper-Lecithin.

A. Strauss has introduced a new process of treatment, the so-called Finkler method of treatment with copper-lecithin, into the therapy of epithelioma; it was first described by the Countess of Linden and E. Meissen. According to Strauss, copper-lecithin is a combination of lecithin and copper chloride, containing 4.5 p. c. of copper. The three cases described by the author, two cases of pure epithelioma and one case of primary lupus, were treated with an ointment which was prepared from copper-lecithin and alcohol without the employment of fat. The curative action of this ointment depends in the first place on the action of the copper salt; it cannot yet be said with certainty whether the lecithin component also takes part in the action. But it is quite possible, when it is considered that choline, a product of decomposition of lecithin, as was found by Werner and Schwarz, is capable to a certain extent of substituting X rays, and that choline itself has received consideration in the treatment of cancer\*). The results obtained by Strauss in the local employment of copper-lecithin will perhaps lead to the investigation of the chemo-therapeutic action of the new drug in carcinoma, in the form of injections, enemata and inunctions.

An ulcerating epithelioma, about the size of a lentil, which was not healed with cauterisation by solid carbonic acid, was cured within a week by treatment with copper-lecithin. The second case, an ulcer at the angle of the nose, which had been present for two years and had been diagnosed

Strauss, Deutsche medizinische Wochenschrift 1912, No. 45, p. 2122.  
Linden, Beiträge zur Klinik der Tuberkulose Vol. 23, No. 2. —

Zentralblatt für die gesamte Arzneimittelkunde 1912, No. 8/9,  
p. 401.

Meissen, ibidem.

Werner-Schwarz, Compare Merck's Report 1907, p. 74.

\* ) Compare the article on Choline in this Report.

as squamous - celled carcinoma, cicatrised in the course of two months. The third case, probably a lupus-carcinoma of the nose, which had been treated in vain for years, also showed a tendency to healing and cicatrisation of the ulceration.

In a further communication on his chemo-therapeutic work, Strauss speaks of preparations which he describes as combinations of inorganic or complex copper salts with lecithin. He used them with and without the addition of methylene blue iodide (the hydriodic acid salt of methylene blue) in lupus and external tuberculosis. For general treatment, the most suitable preparation, according to the author, is a solution prepared from a complex copper salt (with or without lecithin), which is given by intramuscular injection. The ointments also proved useful. The copper-lecithin preparations are administered internally in the form of capsules and pills, and iodine methylene blue in capsules.

According to the author's instructions, small doses are given at first, especially to sensitive patients; 0.25 to 0.5 c. c. is given and increased to 1 c. c., which contains 0.01 grammie ( $\frac{1}{6}$  grain) of copper; for intravenous injection up to 0.1 grammie ( $\frac{1}{2}$  grains) in 10 c. c. of water. At first two injections a week are given, later one injection. Inunction cures should be carried out like mercury cures, 3 to 5 grammes (45 to 75 grains) being used daily. Apart from transient cutaneous irritation, they give rise to no ill effects. For internal treatment, pills, capsules or tablets are given once to three times a day after food, according to the amount of copper they contain. Local treatment is just as simple as general treatment. In large areas of lupus it is best to treat isolated areas, especially in very sensitive patients. Ointments are either energetically rubbed in 2 to 3 times a day, or they are applied spread on gauze. To alleviate pain, heroin or morphine is given for a few days. When a reaction has occurred, the following ointment is to be prescribed for healing purposes: Rp. Bismuth. subgall. 3.0 grammes (45 grains), Liquor alumin. acetic. (20 p. c.) 3.0 to 6.0 grammes (50—100 min.), Eucerin. anhydric. ad 30.0 grammes (1 oz). 10 p. c. of cycloform may be added to this ointment. When the reaction has been checked by this ointment, the cure is to be repeated until all infiltrations have disappeared. This local method of treatment

is especially indicated in lupus. In a few cases of erythematous lupus these drugs failed, but the local treatment of epithelial cancer gave good results.

Meissen tried copper-lecithin and methylene blue iodide in pulmonary tuberculosis and found that these drugs were of service in the second stage of the disease. The two preparations were injected subcutaneously, viz., 2 to 5 c. c. of a 2 to 3 p. c. solution of methylene blue iodide, and 0·5 to 1 c. c. of a 1 to 2 p. c. solution of copper-lecithin twice a week. The results were very satisfactory in 80 p. c. of the cases treated and in some they were surprisingly good. The treatment should be continued for 2 to 3 months. It leads to the subsidence of the fever and to the improvement of the local signs, and soon renders the expectoration free from bacilli.

According to a communication by R. Kobert, the treatment of tuberculosis, scrofula and lupus by copper preparations, which has not as yet been regarded with favour in Germany, may be expected shortly to play an important rôle, thanks to the work of Strauss mentioned above. It may therefore be pointed out that cupro-hæmol, introduced by Kobert, is very suitable for this purpose. It may be given internally without harm in doses of 0·1 to 0·5 grammes ( $1\frac{1}{2}$  to  $7\frac{1}{2}$  grains) in chocolate powder, etc., several times a day. Or it may be given, emulsified with lecithin, by intramuscular injection, or applied locally to lupus in the form of an ointment with methylene blue iodide.

### Copper Sulphate.

In osteo-periostitis with fistula formation, A. Campani used irrigations of copper sulphate solution with good results. He reports upon 29 cases which were cured by his method of treatment, among them two in which amputation had been contemplated. According to the author's instructions, the fistulas are irrigated for 3 to 4 minutes with a 4 to 5 p. c. aqueous solution of copper sulphate. The solution should be used as hot as it can be borne. The method is applicable to tuberculous and non-tuberculous suppuration, so long as the seat of suppuration is sufficiently accessible.

Kobert, Direct communication.

Campani, Gazzetta degli ospedali e delle cliniche 1912, No. 59.

— Klinisch-therapeutische Wochenschrift 1912, No. 42, p. 1244.

A simple spectroscopic test for hemibilirubin (identical with urobilinogen) is described by H. Fischer. One litre of the pathological urine to be tested, which shows a fairly marked Ehrlich's aldehyde reaction, is shaken up with 50 c. c. of chloroform. When the chloroform has separated, it is drawn off by means of a separating funnel, and the emulsion which may have formed is destroyed by means of talc powder. Thereupon the chloroform extract is filtered through paper moistened with chloroform into a small separating funnel and is shaken up with 3 to 5 c. c. of  $\frac{1}{10}$  normal caustic soda solution. This is filtered and to it are added 1 to 2 drops of a 10 p. c. solution of copper sulphate and then 8 to 10 drops of a 33 p. c. caustic soda solution. A pale lilac coloration results, which darkens perceptibly and after at most 2 minutes shows spectroscopic bands in the red, yellow and blue. The band in the red is specially typical of hemibilirubin. The spectroscopic result is more clearly seen if the alkaline solution is acidified with acetic acid and then shaken up with 3 to 4 c. c. of chloroform and this solution in chloroform is employed.

Compounds of copper appear to be gaining in therapeutic interest in the treatment of carcinoma. Thus, besides copper-lecithin, which is described above, so-called colloid copper hydroxide, the "cuprase" of Gaube, has been introduced into therapeutics. According to him, the preparation is supplied in ampoules containing 5 c. c., corresponding to 0.00121 gramme of copper. Judging by his results, the author thinks himself justified in assuming that cuprase, when injected intramuscularly or subcutaneously, is capable of curing malignant tumours. The injections are said to be painless and to alleviate the pain caused by the tumour. The new drug is, at any rate, worthy of further trial.

### Coryfin.

In a paper on the value of menthol and its derivatives in the treatment of affections of the upper air passages, A. Heindl draws special attention to coryfin (ethyl-glycolic

Fischer, Münchener medizinische Wochenschrift 1912, No. 47, p. 2555.

Gaube, Repertoire de pharmacie 1912, p. 453. — Schweizer Wochenschrift für Chemie und Pharmazie 1912, No. 48, p. 718.

Heindl, Aerztliche Reformzeitung 1912, No. 8, p. 97.

ester of menthol). As the taste of this preparation is not agreeable to all patients, cases requiring the prolonged employment of the drug, as for instance acute rhinitis, may, in his experience, use 5 to 10 p. c. coryfin-cotton wool, which can be frequently introduced into the nostrils and left there for some time. Adults and children even more may, according to the author, obtain benefit from instillations and sprays of a 25 to 50 p. c. coryfin solution in liquid paraffin, or from the application of coryfin ointments (which may naturally be weaker), especially if these are used before going to sleep and before going out. The patient does not easily become a temporary mouth-breather. A mixture of 25 p. c. of coryfin in liquid paraffin and 3 p. c. of cycloform also gives relief. Apart from rhinitis, coryfin is also useful in affections of the upper air passages, if it is used for painting the throat or in the form of insufflations. The dryness, the burning and the hyperæsthesia of the mucous membrane soon pass off, the crusts are loosened, and the redness and swelling of the mucous membrane and the desire to cough disappear. For inhalation by means of a spray, Heindl usually employs a 0·5 p. c. coryfin emulsion in liquid paraffin, to which may be added bitter almond water, cocaine, alypin, morphine, etc. Heindl also uses coryfin in 25 to 50 p. c. solution for painting the naso-pharynx in cases of extreme dryness and crust formation, and also in diabetes and other dyscrasias. In laryngeal tuberculosis a solution of 1 gramme (15 grains) cycloform in 25 grammes (1 oz) of coryfin has proved of special value.

It has recently been pointed out that menthol and its derivatives, which are somewhat widely used in acute coryza, may, particularly in children, give rise to secondary effects, for which reason care is required when using them. W. Lublinski therefore only prescribes 5 to 25 p. c. coryfin solutions in liquid paraffin, which may be instilled into the nose in doses up to 10 drops and then distributed by light massage. For children under 8 to 10 years of age, it is safer only to use coryfin ointments, in which the coryfin content does not exceed 2 p. c. The nasal employment of coryfin is not to be recommended in children under 2 years of age. The author reports a case in which the application of quite a small amount of a 2 p. c. coryfin ointment to a

child aged 11 months caused spasm of the glottis and other disquieting symptoms\*).

### Creosotal.

G. Hunaeus records his experiences with the employment of creosotal\*\*) in practice among children. According to him, it not only dissolves the products of secretion of the diseased mucous membranes, but also possesses a direct bactericidal action. Its influence in lowering the temperature was particularly marked; often, after a single dose, the temperature was lowered by 1 to 1.5° C. If the medication was continued sufficiently long, the temperature returned to normal by lysis, but if discontinued too soon, it rose again. The author therefore considers that not a single dose of the medicine should be omitted, but would have it continued in small doses until every auscultatory sign has disappeared. The severe general symptoms of pneumonic intoxication, such as somnolence, delirium and spasm, usually disappear after 12 to 24 hours. Hunaeus was convinced of the favourable influence of creosotal, especially in the severe and obstinate broncho-pneumonias following measles, and he frequently gave it as a prophylactic immediately on the appearance of Koplik's spots. He thus brought about the much more rapid disappearance of bronchitic symptoms, and without diarrhoea, which so often accompanies measles.

The action of creosotal was particularly favourable in chronic bronchitis which had defied all the usual hydro-therapeutic and remedial measures. It is also useful in whooping-cough complicated by broncho-pneumonia. It has, however, no effect on the number and severity of the attacks.

The drug should, according to the author, be given in relatively large doses, and also to young babies. In his experience, it may be prescribed without apprehension in the following doses: In the first year of life 5 drops = 0.5 grammes 3 times a day; in the second year of life 10 drops = 1 grammme 3 times a day; in the third and fourth years 15 drops = 1.5 grammes; in the fifth and sixth years 20 drops = 2 grammes; and from the seventh to the tenth year 25 to

\*) Compare the article on Menthol in this Report.

\*\*) Compare Merck's Report 1904, p. 117.

Hunaeus, Medizinische Klinik 1912, No. 39, p. 1586.

30 drops = 2.5 to 3 grammes. After the disappearance of the auscultatory signs, the drug is continued in half doses for another week, in order to prevent relapses.

### Diaspirin.

Like aspirin, diaspirin\*) is also said by A. Eysell to be of value at the commencement of a "cold". The author only prefers diaspirin because it is better tolerated by the intestinal tract. In his opinion, 1 gramme (15 grains) of diaspirin should be taken when the signs of an approaching "cold" become manifest, and the dose should be repeated in 6 hours. By giving 3 grammes (45 grains) on each of the two following days, the author was always successful in cutting short the "cold". He usually gave his patients 0.5 grammes ( $7\frac{1}{2}$  grains) morning and noon, and 1 gramme (15 grains) in the evening. If the action did not set in promptly, he increased the daily dose to 3 grammes (45 grains). Eysell has also obtained very good results with diaspirin at the commencement of acute inflammation of the throat and tonsils. He is convinced that by means of this medication he has frequently saved his patients from peritonsillitis and articular rheumatism.

## Digitalis Substances.

### Digitalis Leaves.

The action of digitalis\*\*) and its nature has been discussed by W. Heubner, Bickel and Tsividis, Brandenburg and Hoffmann, Schrenk and E. Edens. Their work, which is both important and interesting, theoretically and practically, can only be referred to here, as it cannot well be abstracted with the requisite exactitude. Those interested in the biological tests for digitalis should refer to the com-

\*) Compare Merck's Report 1908, 1909 and 1910.

Eysell, Münchener medizinische Wochenschrift 1912, No. 37, p. 2031.

\*\*) Compare Merck's Report 1911, p. 31-58.

Heubner, Therapeutische Monatshefte 1912, No. 3, p. 157.

Bickel-Tsividis, Biochemische Zeitschrift 1912, Vol. 45, p. 462.

Brandenburg-Hoffmann, Therapeutische Monatshefte 1912, p. 61.

Schrenk, Münchener medizinische Wochenschrift 1912, No. 53, p. 2908.

Edens, Deutsches Archiv für klinische Medizin 1911, Vol. 104, p. 512.

munications of Burmann, Weiss, Focke, Hartung, Lhoták von Lhota and Niculescu.

A publication by R. Kobert, dealing with the active principles of digitalis and the method of prescribing it, is also of special interest. According to him, gitalin\*), digitoxin and digitalinum verum may be considered the most active glucosides of digitalis (compare Merck's Report 1911). According to Kobert, no digitoxin is present in digitalis infusion, wherefore its efficacy must be due to some other principle, and this the author considers to be gitalin. This glucoside is presumably the component of digitalis of most therapeutic importance, but it is not yet on the market. It is to be prescribed in solution 0·01 in 10·0, drop by drop, in gradually increasing doses, until the action has been attained which is usually effected by the infusion. Only after a careful clinical study has been made of gitalin, does Kobert recommend that it should be combined with the saponin substance, digitsaponin, which is present in digitalis infusion; and tests can then be carried out to show whether the combined action is better than that of gitalin by itself. The fact that digitalis pills are more efficacious than the infusion is due to the pills being prepared from freshly powdered leaves, so that they contain digitoxin as well as gitalin. Digitoxin, which is prepared by me in a pure condition and is also supplied in the form of tablets, is recommended by Kobert to be taken alternately with the infusion, in order that the full effect of the leaves may be obtained. The maximum dose of 0·2 gramme (3 grains) of the leaves corresponds to 2 tablets of

Burmann, Bulletin de la société chimique de France 1912, Vol. 11, p. 221. — Schweizer Wochenschrift für Chemie und Pharmazie 1912, No. 51, p. 757.

Weiss, Das österreichische Sanitätswesen 1912, 30<sup>th</sup> May, Supplement to No. 22. — Pharmazeutische Praxis 1912, No. 7—9.

Focke, Therapie der Gegenwart 1912, No. 8, p. 379.

Hartung, Archiv für experimentelle Pathologie 1912, Vol. 69, p. 149.

Lhota, Archives internationales de pharmacodynamie et de thérapie 1912, Vol. 22, p. 61.

Niculescu, Zeitschrift für experimentelle Pathologie und Therapie 1912, Vol. 11, p. 277.

Kobert, Münchener medizinische Wochenschrift 1912, No. 34, p. 1864.

\*) Gitalin and Digitalein cannot be considered as being identical. Gitalin is soluble in water 1 in 600, and in chloroform in all proportions; while digitalein is readily soluble in water and practically insoluble in chloroform.

0.00025 gramm (1/250 grain) of digitoxin each. The action of digitalis seeds can be replaced in an analogous manner if gitalin solution be given alternately with tablets containing 0.00025 to 0.002 gramm (1/250—1/32 grain) of digitalinum verum. As soon as gitalin can be prepared in a perfectly pure state, it will be possible with these three substances, gitalin, digitoxin and digitalinum verum, according to Kobert, to be independent of the varying content and of the consequent varying action of digitalis leaves and digitalis seeds.

Hitherto an attempt has been made to avoid these variations by using so-called folia digitalis titrata. Their significance is explained by Focke in a comprehensive communication. Another modern digitalis preparation is "Digitalis Winckel" or "Corvult", dried digitalis leaves, freed from ferment by a special process, and hence said to keep particularly well. A. Jodlbauer has found that by the conservation of the preparation, which is also on the market in the form of tablets, its therapeutic efficacy is not diminished.

H. F. Grünwald has reported on the cumulative action of digitalis. In so-called "circulatory experiments", he found that by the employment of a solution of 1.5 to 2 milligrammes of gitalin (Germanicum Merck) in 50 grammes of Ringer's solution, the commencement of poisoning takes a longer time as the solution passes from heart to heart, e. g., that storage takes place in the hearts which are first reached. The manner in which the heart stops also changes; the first heart alone stops beating in systole, the following ones more and more nearly in diastole. The author also established the fact that poisoning did not depend upon the concentration of the solution which flowed through the heart. Rather is the heart capable of selectively taking up the amount of poison necessary for poisoning from very low concentrations.

In emphysema and nephritis of advanced age, according to A. Mayor, the administration of small doses of digitalis leaves is valuable as a prophylactic measure against the possible setting in of cardiac debility. According to his instructions, for this purpose a daily dose of 0.1 gramm (1½ grains) of

Focke, Therapie der Gegenwart 1912, No. 5 and 6.

Jodlbauer, Münchener medizinische Wochenschrift 1912, No. 4, p. 200.

Grünwald, Archiv für experimentelle Pathologie 1912, Vol. 68, p. 231.

Mayor, Presse médicale 1912, p. 77.

powdered leaf is given for 3 days, and a week's interval is allowed to elapse before repeating the medication.

M. Hilferding, in a series of cases, succeeded in favourably influencing troubles connected with pregnancy by the administration of digitalis. The troubles, which consisted of headache, vertigo, nausea and vomiting, were cured or improved in almost every case. Five tablespoonfuls of a digitalis infusion 0·6—1·0 in 200·0 were administered daily.

### Digitalis Tincture.

Kobert suggests that digitalis tincture be prepared from fresh leaves and 96 p. c. alcohol. If the leaves, immediately after gathering, are covered with 10 times their weight of alcohol, the action of the ferments is completely suppressed, and there is the possibility that digitoxin and other substances insoluble in water may go into solution. The tincture, when ready, should be kept in small bottles of amber-tinted glass, completely filled and tightly corked. The use of the ethereal tincture cannot be recommended, as ether does not increase the solubility of the active principles in question. Kobert states that fluid extract of digitalis, dialysatum digitalis, and tinctura digitalis ab oleo et acido liberata, which is very troublesome to prepare, are less stable. "Digitalon is a fluid which contains chloretone and which cannot therefore be reckoned among the pure digitalis preparations. The same applies to digistrophan. I consider both to be superfluous." His opinion on digalen is that it does not merit the designation "Digitoxin solubile". It is, in the author's opinion, a cleverly made aqueous extract of digitalis, of the stability of which he has no experience.

The importance of Kobert's aim to prepare a stable digitalis' tincture is shown by the results of A. Goodall's investigations. He found marked variations in efficacy in a series of digitalis tinctures and he showed that the stability may vary greatly. P. Moran came to practically the same conclusion. Only when prepared from carefully dried leaves of

Hilferding, Petersburger medizinische Wochenschrift 1912, No. 2, p. 31.

Kobert, Münchener medizinische Wochenschrift 1912, No. 34, p. 1867.

Goodall, British Medical Journal 1912, I, p. 887.

Moran, Medical Chronicle 1911, October. — Deutsche Medizinal-Zeitung 1912, No. 8, p. 132.

a good quality and carefully preserved, may a tincture be reckoned on which will retain its efficacy for 2 to 3 years. The author further points out that by the employment of 90 p. c. alcohol a more efficacious tincture is obtained than when dilute alcohol is used.

### Digifolin.

Digifolin is an extract freed from superfluous and perhaps injurious substances present in digitalis leaves; it is issued in the form of tablets and of solutions in ampoules. According to H. Hartung, the solution contains all the glucosides of digitalis which act upon the heart, with the addition of water and a little sodium chloride. Pharmacological investigations on frogs showed that digifolin possesses the full action of digitalis. The contents of a digifolin ampoule correspond in strength approximately to a 10 p. c. infusion, so that they are of the same strength as 0·1 grammme ( $1\frac{1}{2}$  grains) of digitalis leaves. The tablets are of similar strength.

L. Silberstein, B. Moore and H. Rosin have reported upon **Digalen\***). They used the drug intravenously with benefit in mitral insufficiency, cardiac asthma, etc.

According to J. Fürthmaier, digalen is a specific in haemoglobinæmia of horses, and this is confirmed by Kofler and Kubaschewski. According to the instructions of these authors, in the presence of great restlessness and of sweating, the animals are first given 0·5 grammme ( $7\frac{1}{2}$  grains) of morphine hydrochloride, and when they have become calm, a subcutaneous injection of 15 grammes ( $\frac{1}{2}$  oz) of digalen. After 2 to 4 hours the animals rise and remain standing quietly. The injection need only exceptionally be repeated. The dark colour of the urine disappears without further treatment.

**Digipuratum** is a useful and reliable drug, which has been several times dealt with in my Reports. Favourable opinions

Hartung, Münchener medizinische Wochenschrift 1912, No. 36, p. 1944.

Silberstein, Therapeutische Monatshefte 1912, No. 2, p. 120.

Moore, British Medical Journal 1912, I., p. 60.

Rosin, Deutsche medizinische Wochenschrift 1912, No. 16, p. 739.

\*) Compare Merck's Reports 1904—1911.

Fürthmaier-Kofler, Tierärztliches Zentralblatt 1912, No. 23.

Kubaschewski, Berliner tierärztliche Wochenschrift 1912, No. 51.

upon this drug have been expressed by M. Hedinger, E. Hail, W. J. Beresin, L. v. Siebenrock, Michaud, and R. G. Wiener.

Hail found in digipuratum a digitalis preparation which is distinguished for its high potency and exact dosage. If rapid action is required, it acts promptly and reliably in the form of intravenous or intramuscular injections. In the treatment of chronic disease it may be recommended because it is well tolerated. It is noteworthy on account of its diuretic action, when used in combination with diuretin in nephritis and uræmia. Hedinger expresses himself in similar terms. Even when small doses of diuretics were given, such as 0.5 gramm (7½ grains) of diuretin, the author noticed a marked action if 0.1 gramm (1½ grains) of digipuratum was administered simultaneously. The readiness with which the drug is tolerated is confirmed by von Siebenrock. He gave relatively large doses, which were as a rule tolerated by the stomach without the least trouble. Intramuscular and intravenous injections may be recommended on account of their rapid action, whereas the subcutaneous application is better avoided on account of its irritative effects. If necessary, 4 to 6 c.c. of digipuratum may be given at a time by intramuscular injection. For sensitive patients 0.01 gramm (1/6 grain) of morphine hydrochloride may be added to each injection, but for others this is not necessary, as intramuscular injection is not particularly painful if the correct technique is employed. 2 to 3 c.c. are enough for intravenous application. Wiener has also prescribed digipuratum with benefit in myocarditis, chronic endocarditis, chronic cardio-nephritis, cardiac dilatation, dyspnoea, oedema, anasarca, and weak, irregular pulse. In pneumonia it always strengthens the action of the heart.

Beresin has tested digipuratum pharmacologically, and biologically, and has found it to possess the full action of

Hedinger, Münchener medizinische Wochenschrift 1911, No. 44, p. 2353.

Hail, Dissertation Erlangen 1912.

Beresin, Russky Vratsch 1912, No. 3.

Siebenrock, Klinisch-therapeutische Wochenschrift 1912, No. 9, p. 261.

Michaud, Münchener medizinische Wochenschrift 1912, No. 8, p. 444.

Wiener, Merck's Archives 1911, No. 12.

digitalis. The results of the pharmacological investigations of Gottlieb and Ogawa supply an experimental basis for the clinical observation that digipuratum, in proportion to its strength of action, disturbs the digestive organs less than digitalis leaves. The active principles of digitalis are far more rapidly absorbed from digipuratum than from the leaves. The author's experiments have shown that a dose of digipuratum irritates the gastric mucous membrane less than does the same or even a smaller dose of folia digitalis titrata or its infusion.

### Digitsaponin.

To the saponin-like substances of digitalis are reckoned, as I pointed out in my Report last year, the two digitonins, digitonin Schmiedeberg, an amorphous body soluble in water, and digitonin Kiliani, a crystalline body, almost insoluble in water. According to the present view, both are contained in digitalis seeds, but not in digitalis leaves. Two highly interesting papers by R. Kober and Kraft throw light upon the chemistry of these digitalis saponins.

Kraft has isolated 3 digitsaponins from digitalis leaves, viz., 1.  $\alpha$ -digitsaponin, soluble in 10 parts of boiling alcohol and in 100 parts of cold alcohol, and in all proportions in methyl alcohol. — 2.  $\beta$ -digitsaponin, soluble in 150 parts of hot alcohol, in 250 parts of cold alcohol and in all proportions in methyl alcohol. — 3.  $\gamma$ -digitsaponin, practically insoluble in absolute alcohol, and soluble in methyl alcohol in the proportion of 1 in 30. The difference between these three bodies, according to Kraft, is due to the varying amounts of water they contain. The two soluble forms can be converted into the form which dissolves with difficulty, both by heating and by treatment with alcohol. All three modifications form the same products of decomposition on hydrolysis. The body in question is therefore considered by Kraft to be identical with Schmiedeberg's amorphous digitonin. In opposition to the view held hitherto, the leaves of digitalis would thus also

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Gottlieb-Ogawa, Münchener medizinische Wochenschrift 1912, No. 42 and 43.

Kober, Berichte der deutschen pharmazeutischen Gesellschaft 1912, No. 4, p. 236.

Kraft, Archiv der Pharmazie 1912, No. 2, p. 121—126.

contain digitonin. But Kobert's investigations show that Kraft's digitsaponin cannot be identical with Schmiedeberg's digitonin, because Schmiedeberg's digitonin possesses a powerful haemolytic action, which is not possessed by Kraft's digitsaponin. According to Kobert, digitalis leaves certainly contain saponin or saponins, but these are free from haemolytic properties, which makes them of particular significance in therapy, because like all saponins which are themselves insoluble, they are capable of bringing active principles into solution or pseudo-solution. Added to this, they are not poisonous, as are many other saponins. Thus, while haemolytic tests show digitalis seeds to be active, the leaves prove to be inactive. Their saponin only becomes haemolytic after conversion into saponin.

W. Frieboes, a pupil of Kobert's, pointed out as early as 1903 that saponins, and especially the non-poisonous guaiac-saponin, possess the property of rendering insoluble digitalis glucosides soluble. This fact was confirmed by the experiments of I. Postojeff, in which the author showed that the action of digitoxin (Merck) suspended in Ringer's solution was markedly increased by the addition of a small amount of quillaia-sapotoxin.

### Gitalin, Gitin and Digin.

The preparation and properties of gitalin are described by Kraft. According to him, this glucoside is an amorphous, white powder, unchanged by exposure to air, with a neutral reaction, melting point 150 to 155° C. It dissolves in water in the proportion of 1 in 600, and in chloroform in all proportions. It is also soluble in other organic solvents, for example ether, but then soon undergoes decomposition. Gitalin, after solution in alcohol and the addition of definite amounts of water, is obtained in the form of its hydrate, so-called gitalin hydrate. This is crystalline and melts at 75° C. It is much less readily soluble in water and alcohol than is gitalin. As far as I know, clinical or therapeutic experiments have not yet been carried out with these new digitalis bodies, and they are not yet on the market.

Frieboes, Merck's Report 1903, p. 88.

Postojeff, Biochemische Zeitschrift 1911, Vol. 36, p. 335.

Kraft, Archiv der Pharmazie 1912, No. 2, p. 126.

In a few experiments on frogs, W. L. Symes found that gitalin first effects an increase in cardiac activity, which is transitory and is soon followed by a marked depression, with lengthening of diastole. After the elimination of the gitalin, the heart recovers completely. Gitalin has no haemolytic action.

A newer digitalis substance, which Kraft has obtained from digitalis leaves, is the glucoside gitin. It crystallises in fine needles, melting at about 265° C. with charring; they are soluble with difficulty in alcohol and methyl alcohol, and insoluble in water, benzol and chloroform. According to Schmiedeberg, the preparation is physiologically inactive. A similar, but not identical glucoside, obtained from digitalis leaves, is described by Tambach and named digin. Like gitin, it gives no coloration with Kiliani's reagent. It crystallises in needles, which melt between 271° and 273° C., forming a yellowish-brown liquid.

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#### Dimethylamido-Azobenzol.

This azo-dye\*), used as an indicator in chemical analysis and as a colouring matter for fats, is recommended by A. Friediger for the microscopic demonstration of fats in the gastric and intestinal contents. If, for example, an alcoholic solution of dimethylamido-azobenzol, which has been rendered slightly acid with hydrochloric acid, is added to gastric contents, the fat is stained a brilliant yellow. In the examination of faeces, acetic acid is added, or a mixture of equal parts of a solution of dimethylamido-azobenzol and 30 p. c. acetic acid is used, 1 to 2 drops of which are added to the preparation of faeces, which is then warmed. The heated mass is then examined microscopically for stained fat droplets. But, as formed elements may occur in the stools and gastric contents, which have a yellow colour of their own, it is better to use the following mixture:

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Symes, Journal of Physiology 1912, Vol. 44, 8<sup>th</sup> June.

Tambach, Pharmazeutische Zentralhalle 1912, No. 15, p. 392.

\*) Compare Merck's Index 1910, p. 96.

Friediger, Münchener medizinische Wochenschrift 1912, No. 52, p. 2865.

Concentrated alcoholic solution of dimethylamido-azobenzol

Absolute alcohol

0·5 p. c. alcoholic solution of eosin (70 p. c. alcohol)

Concentrated acetic acid aa 2 c. c.

Lugol's solution (0·5 grammes of iodine and 2 grammes of potassium iodide in 20 grammes of glycerin)  
20 drops

Mucicarmine (concentrated aqueous solution) 20 drops.

It forms a Bordeaux-red solution, which should be perfectly clear. If precipitates form, it must be filtered. To carry out the test, the object to be examined is placed on a slide and covered with a coverslip. The adherent fluid is removed by light pressure on the coverslip and by the use of filter paper. Then the object is stirred up with a little of the stain and the excess is again removed from under the coverslip by means of filter paper. Under the microscope the following picture is observed. The fat is stained a citron-yellow to ochre colour, the starch pale violet to deep blue, and muscle fibres orange to deep carmine. Yeast cells and sarcinæ are stained like muscle fibres, but are easily recognised by their form. Jaworowski's corpuscles remain unstained. Mucin is stained pink to carmine by the mucicarmine.

#### p-Dimethylamido-Benzaldehyde.

In the serum treatment of diphtheria, F. Umber has observed the appearance of scarlatiniform serum exanthemata in a large number of cases. Some of them presented a serious clinical picture, and were indistinguishable from ordinary scarlet fever by clinical examination alone. These exanthemata behaved exactly like a true scarlatinal rash including regional distribution, scarlatinal tongue, glandular enlargement, fever, etc. As the distinction of this serum scarlet fever from true scarlet fever is of importance on account of the danger of infection, the method suggested by Umber should prove of general interest. The author found that by the help of Ehrlich's dimethylamido-benzaldehyde reaction it is possible to distinguish serum scarlet fever from true scarlet fever with a sufficient amount of accuracy. A positive Ehrlich reaction, which is carried out with fresh urine, may be recog-

nised, as is well known, by an intense red coloration. According to the author, it occurred in 96 p. c. of the cases of true scarlet fever and was not observed in a single case of serum rash. The diagnostic significance of the reaction is thus manifest. The technical details are as follows:

2 grammes of p-dimethylamido-benzaldehyde are triturated in a porcelain mortar with 30 grammes of concentrated hydrochloric acid, diluted with 70 grammes of water and filtered. A few drops of this reagent are added to a fresh specimen of urine. If the mixture is coloured red, either at the ordinary temperature or on heating, and if the spectrum shows a definite absorption band in the orange between D and E, the reaction is positive, and the presence of scarlet fever may be considered proved. The positive reaction depends upon the presence of urobilinogen in the urine in scarlet fever.

The employment of the diazo-reaction\*) in place of the reaction just described cannot be recommended, since Woody and Kolmer, as a result of their experiments, at most consider a negative result to be of diagnostic value. They only obtained a positive reaction in 17 p. c. of cases of scarlet fever.

A. Jonass, as a result of experiments with Ehrlich's dimethylamido-benzaldehyde reaction, considers it to be of certain diagnostic significance for the degree of capacity for work of the heart, and as a functional test of cardiac power in certain forms of circulatory disturbance after forced labour. Reference should be made to the author's original work, as it does not lend itself to a brief abstract.

### Dimethyl-Aniline.

The hydrogen of dimethyl-aniline,  $C_6H_5 \cdot N(CH_3)_2$ , which occupies the para position to the  $N(CH_3)_2$  group is, as is well known, readily replaced under the influence of nitrous acid by the nitroso-group (-NO), giving rise to the strongly coloured p-nitroso-dimethyl-aniline hydrochloride. This fact is utilised by E. H. Miller in testing for nitrous acid and for its colorimetric estimation. As a reagent, a solution of dimethyl-aniline hydrochloride is used, which is prepared by dissolving 8 grammes of dimethyl-aniline and 4 grammes of hydrochloric

\*) Compare Merck's Reagenzien-Verzeichnis 1908, p. 68.

Woody-Kolmer, Archives of Pediatry 1912, p. 12.

Jonass, Wiener klinische Wochenschrift 1912, No. 10, p. 375.

Miller, The Analyst 1912, Vol. 37, p. 345.

acid in 100 grammes of water. If to 50 c. c. of the solution to be tested, 1 drop of hydrochloric acid and 3 drops of reagent are added, a yellow colour appears, which is more or less intense, according to the amount of nitrous acid present, and which reaches its highest intensity in the course of 15 to 30 minutes. For the colorimetric estimation a comparison fluid is required, which contains 0·01 gramme of  $N_2O_3$  (in the form of sodium nitrite) to a litre. The presence of nitric acid does not interfere with the reaction, by which one part of  $N_2O_3$  in 1 million parts of fluid can be clearly demonstrated.

### Dimethyl-Glyoxim.

In estimating the content of nickel in steel, P. Slawik discovered a sensitive reaction, depending upon the action of dimethyl-glyoxim on ferrous salts. If one drop of a solution of ferrous oxide is added to a little tartaric acid, and after mixing, 1 c. c. of an alcoholic solution of dimethyl-glyoxim and an excess of ammonia are added, an intense red coloration results. The reaction is said to be superior in sensitiveness to all former ferrous oxide reactions, but it disappears when the iron is oxidised by exposure to the air. A difficulty is, however, experienced in testing for very small amounts of ferrous oxide, because on the addition of ammonia to the acid solution they are very rapidly oxidised by the air.

On the other hand, dimethyl-glyoxim is more and more gaining in favour for the estimation of nickel\*). Wunder and Thüringer describe a process for the separation of nickel and palladium, which is carried out as follows. The liquid to be analysed is rendered faintly acid with hydrochloric acid, and an excess of a 1 p. c. solution of dimethyl-glyoxim in hydrochloric acid (2 p. c.) is added. This is left for half an hour on the water bath, and the precipitate of  $Pd(C_4H_8O_2N_2)_2$  which forms is separated by filtration, washed with boiling water, dried and incinerated. The residue of metallic palladium is then weighed. The filtrate is rendered alkaline by ammonia at boiling temperature in the usual way, and the nickel is weighed in the form of nickel dimethyl-glyoxim.

Slawik, Chemiker-Zeitung 1912, No. 6, p. 54.

\*) Compare Merck's Reports 1905, 1907 and 1910.

Wunder-Thüringer, Annales de chimie analytique et appliquée 1912, Vol. 17, p. 201.

**Dionin.**

Dionin has proved of excellent service in acute coryza, as I have reported before. The striking action of the preparation in cutting short the attack has recently been confirmed by many observers. J. Lindenmayr has also obtained satisfactory results. To diminish the troublesome symptoms, he gave morphine and codeine beforehand; he had to convince himself that relatively large doses of morphine were required (0.02 gramm [ $\frac{1}{8}$  grain] several times a day), which gave rise to a condition of excitement resembling that following intoxication, continuing far into the night and interfering with sleep. The action of codeine, even in doses 0.04 gramm ( $\frac{2}{3}$  grain) was inferior to that of morphine in alleviating the tracheal cough, though it did not give rise to the unpleasant secondary effects caused by morphine. On the other hand, 2 tablets of dionin (0.03 gramm [ $\frac{1}{2}$  grain] each), taken before going to sleep, entirely got rid of the desire to cough. Catarrh of the throat was also cut short by taking 3 dionin tablets in one day. The surprising action of the preparation, according to the author, is due to its influence on the peripheral nerve-endings in the mucous membranes, to its vasoconstrictive property which diminishes hyperæmia, and thus diminishes the desire to sneeze and cough and also diminishes secretion; while morphine acts rather on the central nerve elements, the ganglia, in an unwelcome manner. The author therefore considers dionin a sovereign remedy for "colds" and coughs. Equally satisfactory results were obtained by L. Rabener in bronchial catarrh, pulmonary emphysema and asthmatic attacks, occurring in adults in the spring and autumn, and in pertussis and broncho-pneumonia of children. The author always observed excellent results after a few doses of 0.03 gramm ( $\frac{1}{2}$  grain) (for young children 0.005 to 0.01 gramm [ $\frac{1}{12}$ — $\frac{1}{6}$  grain]).\*)

In ophthalmology, dionin is becoming more and more indispensable. This is shown in the publications which appeared in the past year. Special interest is attached to a new method

Lindenmayr, Berliner klinische Wochenschrift 1912, No. 17, p. 796.  
Rabener, Ärztliche Zentral-Zeitung 1912, No. 7.

\*) To facilitate the employment of dionin, besides tablets containing 0.03 gramm ( $\frac{1}{2}$  grain) of dionin, I now also issue tablets containing 0.015 and 0.01 gramm ( $\frac{1}{4}$  and  $\frac{1}{6}$  grain) of dionin.

of treatment for glaucoma, inaugurated by F. R. von Arlt, which consists in the employment of dionin and pilocarpine. It only comes into consideration in cases requiring immediate treatment and where a powerful action is required, and is carried out as follows:

In glaucoma — while the tear-ducts are continuously compressed — 0.002 gramme ( $\frac{1}{32}$  grain) of (freshly) powdered pilocarpine hydrochloride Merck is introduced by means of a little spoon made to contain this amount. After 8 minutes, 0.005 gramme ( $\frac{1}{12}$  grain) of powdered dionin is introduced by means of another little spoon. This process is repeated at latest in 3 to 4 days. Meanwhile a 2 to 3 p. c. solution of pilocarpine is instilled every 3 hours during the day, until the increase of pressure has totally subsided. From the 6<sup>th</sup> or 8<sup>th</sup> day of treatment the instillation of a 1 p. c. pilocarpine solution once or twice a day is sufficient, and this should be continued for at least a month.

The author's method of treatment differs from former methods in that the dosage of the two alkaloids is higher, and that the dionin is applied 8 minutes after the pilocarpine. The author's purpose is to attain the maximum action of the two drugs almost or quite simultaneously. The case histories given by the author for the cases of glaucoma treated by him speak in favour of his method, so that its further trial may be recommended. P. Greven's test of von Arlt's method in a case of simple glaucoma proved successful. O. Eversbusch, as a result of his experience, also speaks in favour of the method.

In haemorrhagic glaucoma, A. Terson is in favour of conservative treatment in place of enucleation. For the pain he recommends dionin, which always helps and never harms.

P. H. Harry enlarges upon the value of dionin by itself and in combination with other drugs used in eye work, such as atropine. The use of dionin should be specially considered

v. Arlt, Wochenschrift für Therapie und Hygiene des Auges 1912,  
Vol. 15, No. 20 and 21.

Greven, Wochenschrift für Therapie und Hygiene des Auges 1912,  
Vol. 15, No. 40.

Eversbusch. Münchener medizinische Wochenschrift 1912, p. 1234.  
Terson, Wochenschrift für Therapie und Hygiene des Auges 1912,  
No. 44.

Harry, The Prescriber 1912, July.

in all forms of iritis, caused by sepsis, irritation by foreign bodies and toxæmic conditions. After every application of the drug, the vitreous humour becomes clear, the surface of the iris brightens, the spasm of the sphincter of the iris diminishes and any exudation present in the body of the iris is removed. Epiphora and congestion may be increased at first, but photophobia is alleviated and vision improved. The property possessed by dionin of alleviating local and reflex pain also comes into play here in a marked way. But the suitable employment of dionin is a condition of its success, and the prolonged daily use of dionin may cause it to lose the greater part of its stimulating action. The best results are obtained if an interval of 36 hours is allowed between each two instillations. Or a weak solution may be used at first, more or less rapidly passing to concentrated solutions or to the application of powdered dionin. If it is not possible to keep the patient under continuous observation, which may occur with ambulatory cases, it is best, according to Harry, to prescribe a 2.5 p. c. solution of dionin, with instructions to instil it every third day for a fortnight. Then the use of a 5 p. c. solution is prescribed on alternate days for a fortnight. After the application, œdema, congestion and epiphora continue for half to three-quarters of an hour, but the analgesia lasts for hours or days.

With regard to the clearing up power of dionin, no drug, according to Bulson, takes effect so rapidly in intra-ocular haemorrhage as dionin, employed in 5 to 10 p. c. solution. Compared with the great advantages of this treatment, the transient swelling causes the patient only slight discomfort.

Dionin has also proved a valuable drug in the antiseptic treatment of corneal infections, caused by foreign bodies and wounds. After unsatisfactory results obtained by the galvano-cautery and by symptomatic treatment, Nobis has for many years used dionin with benefit. By the employment of dionin-xeroform ointment he always obtained the best visual results, without the help of atropine. In acne rosacea of the cornea (*rosacea corneæ*) dionin, according to Darier, is also bene-

Bulson, Wochenschrift für Therapie und Hygiene des Auges 1912, No. 3, p. 25.

Nobis, Münchener medizinische Wochenschrift 1912, No. 12, p. 662.  
Darier, Clinique ophtalmologique 1912, Vol. 18, p. 2.

ficial. An hour after its application, the author prescribes massage with yellow mercuric oxide ointment or scarlet-red.

A communication by R. Kaz shows that with the help of dionin, operations on the eye may occasionally be avoided. The author reports a case of hypopion keratitis with severe pain and insomnia, in which enucleation had been refused. The eye-ball was of stony hardness, the pus in the anterior chamber was mixed with blood. Treatment by iodoform-eserine ointment, with warm boric acid compresses and the internal administration of sodium salicylate, quinine and phenacetin did not give a satisfactory result. On the other hand, the effect of an ointment containing 0·5 p. c. of physostigmine and 5 p. c. of dionin was extraordinary. On the first day of its employment the pain was relieved to such an extent that the patient dropped into a quiet sleep. Further treatment with the ointment and with daily instillations of pilocarpine solution led to a highly satisfactory result.

M. Ohle mann prescribed dionin ointment in a case of sun-blindness; acuteness of vision was considerably improved and the scotomata disappeared. It is not possible to say whether the restitutio ad integrum observed in this case is to be attributed to the action of dionin, or whether it would have taken place without further treatment. Wolffberg's experience is favourable to dionin, which he found a very useful drug in severe cases of sun-blindness.

A. Dutoit, in a severe case of burning of the conjunctiva, after classical trials with metallic sodium, prescribed frequent eye-baths with a lukewarm, 2 p. c. solution of boric acid, to which dionin and adrenalin had been added in the proportion of 0·5:100. These baths are highly efficacious without being in the least injurious, and they can be repeated more often than can boric-dionin-adrenalin ointments which are otherwise so efficacious.

The work of F. Toczyski on the influence of dionin

Kaz, Wochenschrift für Therapie und Hygiene des Auges 1912,  
Vol. 15, No. 37.

Ohle mann, Wochenschrift für Therapie und Hygiene des Auges  
1912, Vol. 15, p. 287.

Wolffberg, Wochenschrift für Therapie und Hygiene des Auges  
1912, No. 33.

Dutoit, Revue Suisse de Médecine 1912, No. 3.

Toczyski, Zeitschrift für Augenheilkunde 1912, Vol. 28, p. 32. —  
Therapeutische Monatshefte 1912, No. 10, p. 742.

on the behaviour of the pupil and the tension of normal eyes can only be referred to here; and the same applies to a lecture by H. E. Goetz, which has appeared in print and in which a summary is given of the experiences obtained with dionin in ophthalmological practice.

A further confirmation of the experience that dionin is of eminent service in the cure of the morphine habit is given in a publication by R. v. Radesky. The gradual replacement of morphine by dionin and the gradual leaving off of dionin was completely successful in the author's hands and was not felt by his patients. He therefore considers dionin a reliable and harmless drug, which may be used by every physician with a prospect of success.

A communication by K. Rusanow is of interest in veterinary practice. According to him, dionin has proved most useful for its absorbing and clearing properties in eye diseases of domestic animals, e. g., in inflammation of the cornea and diseases of domestic animals, e. g., in inflammation of the cornea and iris, corneal opacity, ulceration of the cornea, etc. Among other cases, he treated parenchymatous keratitis in a horse with instillations of a 5 p. c. solution of dionin, with the result that the opacity disappeared after 4 days, and after a week the cornea became perfectly clear. In a case of iritis, besides cold compresses, he prescribed 2 drops of a solution of dionin-atropine (0·3:0·15:30·0) daily and brought about a rapid cure, so that the horse could be discharged after 12 days.

### Diposal.

The pharmacological investigations carried out by E. L. Tocco showed that diposal\*) remains unchanged for 6 hours in the gastric juice, while it is broken down in 2 to 3 minutes in the duodenal secretion. In the stomach itself, it is only broken down after a long time, for which reason it does not cause gastric disturbances in experimental animals unless doses of 0·5 grammes per kilogramme are given. Its rapid disintegra-

Goetz, Lecture to the Knox County Medical Society on 13<sup>th</sup> February 1912. — Merck's Archives 1912, No. 8.

Radesky, Merck's Archives 1911, No. 12. (December.)

Rusanow, Veterinarny Wratsch 1912, No. 23.

Tocco, Therapeutische Monatshefte 1912, No. 9, p. 671.

\*) Compare Merck's Reports 1908—1911.

tion in the duodenum causes salicylic acid to appear in the urine a short time after taking the drug. The fatal dose for rabbits is 3 grammes and for dogs 1·3 to 1·4 grammes per kilogramme of body-weight. Injury to the kidneys is only observed after large doses. In disturbances of motility, caution should be exercised, as troublesome secondary effects may occur.

G. Campora prescribed diplosal in acute and subacute articular rheumatism, angina, sciatica, neuralgia and muscular rheumatism. His results show that the preparation is serviceable in daily doses of 4 to 6 grammes (60—90 grains). These doses cause no disturbance of the digestive apparatus and have no evident influence on the circulatory and nervous systems; only a slight fall in the blood pressure can be observed. A few nervous patients were troubled with buzzing in the ears. The analgesic action of diplosal is specially noteworthy; it is observed in painful articular affections, neuralgia and myalgia. The pain was also rapidly alleviated by diplosal medication in cases of obstinate sciatica and in the crises of tabes.

A. Schwenk was induced by the success described by Minkowski in cystitis to try diplosal as an antiseptic for the bladder in cystitis, pyelitis and in gonorrhœal and non-gonorrhœal urethritis. The effect of the preparation was frequently striking in cases of chronic cystitis due to hypertrophy of the prostate. The urine became clear and the subjective condition of the patients was improved. In gonorrhœal urethro-cystitis it also assisted in rendering the urine clear and it relieved the troublesome strangury. The author used it as a prophylactic in acute gonorrhœa in order to prevent the extension of the disease to the higher parts of the urinary apparatus. As it may also be beneficial in chronic non-gonorrhœal urethritis, coli-pyelitis, coli-cystitis and tuberculous cystitis, it is deserving of further consideration in urology.

### Dymal.

Dymal, which consists essentially of didymium salicylate, together with cerium salicylate and lanthanum salicylate, is a

Campora, *Clinica medica italiana* 1912, p. 315.

Schwenk, *Dermatologische Wochenschrift* 1912, p. 90.

Minkowski, *Merck's Report* 1908, p. 185.

fine, reddish-white powder, and is recommended by Berliner for the treatment of burns of the second degree. On the trunk and the extremities, the author kept the preparation in place by means of bandages, but on the face he made use of its adhesive and protective properties, and sprinkled more on if uncovered surfaces appeared. Thus it rapidly alleviated pain and brought about healing. Dymal also proved beneficial in intertrigo and ulcers of the leg. In these indications it is of use, not only as a protective, but on account of its stimulating action on the formation of epidermis. Finally Berliner used dymal with benefit in pemphigus neonatorum\*).

### Emetine Hydrochloride.

One of the oldest uses of ipecacuanha root in therapeutics is in amoebic dysentery. The only disadvantage of this drug has always been its emetic action, which is due to its components, emetine and cephæline. The antidyserteric property of the drug, however, was not considered to be due to either of the two alkaloids, but to ipecacuanhic acid. In order to eliminate the emetic action of the drug, the root was almost entirely freed from the alkaloids, and thus is could be administered in relatively large doses. The value of this de-emeticised (and de-cephaelinised) drug in amoebic dysentery was fully corroborated by a number of authors, among whom were Kanthak, Caddy, Kramm, Zemboulis-Eregli. But the hypothesis that ipecacuanhic acid formed the active agent was rendered very doubtful by the investigation of ipecacuanhic acid. I have previously reported that Tokuye Kimura prepared pure ipecacuanhic acid and found that it neither destroyed nor checked the growth of *Bacillus dysentericus*. But as this author did not carry out experiments in amoebic dysentery, no reliable conclusion can be drawn as to the efficacy of the preparation in this disease. Nevertheless, it is a sur-

Berliner, Allgemeine medizinische Zentralzeitung 1912, No. 49, p. 639.

\*) Compare Merck's Reports 1901 and 1908.

Kanthak-Caddy, The Practitioner 1893, May. — Merck's Report 1893, p. 75.

Kramm, Deutsche militärärztliche Zeitschrift 1902, No. 5. — Merck's Report 1902, p. 105.

Zemboulis, Merck's Report 1904, p. 212.

Tokuye Kimura, 1904, p. 217.

prising fact that L. Rogers has recently declared emetine to be a highly efficacious drug, far excelling all the customary drugs employed in amoebic dysentery. The author is justly surprised that the pure alkaloids of ipecacuanha have never been tried in amoebic dysentery. Experiments with emetine are more suitable, because cephaeline is known to possess a stronger emetic action than emetine.

In the first place Rogers carried out experiments with *Entamoeba dysenterica* from dysenteric stools, and found that solutions of emetine hydrochloride act energetically on the amoeba. A 0·01 p. c. solution causes considerable alteration in its microscopic appearance, and even a 0·001 p. c. solution renders it non-motile and apparently kills it. As emetine severely affects mucous membranes, Rogers tried to solve the problem by applying the remedy subcutaneously. Given in this way, according to the author, it does not lead to vomiting and is non-injurious in other ways. The therapeutic effect was so surprisingly good in the author's first experiments that he proceeded to more detailed investigations.

Subcutaneous injections of emetine have proved highly beneficial in the most dangerous form of amoebic dysentery, which occurs as a primary attack or as a sudden exacerbation of chronic disease, which is manifested by extreme thickening of the large intestine, palpable externally, by leucocytosis, gangrene, peritonitis and abscess formation. They have also proved beneficial in cases of medium severity, which can usually be cured by early treatment with ipecacuanha, in chronic dysentery, in acute hepatitis with threatening hepatic abscess and in abscesses of the liver and spleen. In hepatic abscesses, after operative removal of the pus, the author has injected emetine into the tumour with very good results. The injections are so specific in action that they serve to distinguish amoebic dysentery from bacillary dysentery, as emetine is without influence on bacillary dysentery.

For the injections a solution of emetine hydrochloride in water or normal saline solution is used. 0·03 to 0·04 grammes ( $\frac{1}{2}$ — $\frac{2}{3}$  grain) is given for a single or daily dose. The author has given as much as 0·06 grammes (1 grain) without observing vomiting or symptoms of depression. The large doses should, however, only be used for severe cases.

**Enesol<sup>\*)</sup>.**

Frey's investigations, which had shown that enesol exercised a marked effect on the symptoms of meta-syphilitic nervous diseases and especially on the results of the Wassermann test, induced M. Vorbrot and V. Kafka to further study the efficacy of enesol. They directed their attention particularly to the biological behaviour of the cerebro-spinal fluid and of the serum. They were not, however, able to confirm Frey's results. Treatment by enesol had no influence on the clinical aspect of the paralysis. In one case of tabes only was slight improvement of the arthropathy observed. As regards the reactions in the blood and the cerebro-spinal fluid, there was no definite alteration in the cell content of the fluid; rather was the proportion of antibodies increased and in only one case was a diminution observed, which was, however, so slight that, in view of the well known variations in the proportions of antibodies present in the blood, no weight can be attached to it. The same applies, according to the authors, to the presence of haemolysins in the fluid. The authors cannot therefore recommend enesol treatment for general paralysis. As regards tabes and syphilitic diseases of the brain, further investigations are required in order to establish the value of the drug.

L. Meyer does not attach much value to enesol therapy in the treatment of syphilis, because drugs, even if they contain a high percentage of mercury, cannot bring about successful results if, like enesol for example, they are very rapidly excreted by the organism. Even the frequent application of such drugs cannot be expected to effect the syphilitic virus permanently. On the other hand, Thorel obtained very good results by the intravenous application of enesol in various syphilitic affections, which had not responded to treatment by grey oil and injections of mercuric biniodide. According to his prescription, feeble patients are given 6 c.c. on the first day and then 7 to 8 c.c. of enesol solution on alternate days, so

<sup>\*)</sup> Compare Merck's Reports 1904—1911.

Frey, Merck's Report 1911, p. 226.

Vorbrot - Kafka, Berliner klinische Wochenschrift 1912, No. 3, p. 106.

Meyer, Dermatologische Zeitschrift 1912, Vol. 19, No. 4.

Thorel, La Clinique 1912, 2nd February. — Revue internationale de médecine 1912, No. 20, p. 359.

that at the end of 12 days about 1·2 grammes of enesol = 0·45 gramme of mercury, have been given; vigorous patients are given 7 to 8 c.c. on the first day and 8 to 10 c.c. of enesol solution on alternate days, so that in 12 days they receive about 1·5 grammes of enesol = 0·57 gramme of mercury. Both the syphilitic symptoms and the general health were benefited by this treatment, which never gave rise to toxic symptoms.

### Eosin-Selenium.

In order to complete my communications of last year (1911 p. 227), reference will be made to the publications of A. v. Wassermann, F. Keysser, M. Wassermann, F. Nagelschmidt, Thiroloix and Lancien, E. G. Kessler and v. Oefele.

According to Wassermann, after having established the selective action of the selenium oxides or selenium salts on mouse-tumours, a substance was sought which, after the application of these preparations, would enable them to penetrate into the tumour and would hasten their penetration. For this purpose eosin was chosen, because former investigations of the author had shown it to possess well marked powers of diffusion, wherefore it was specially considered as a means of conveying selenium oxide into the organism. Nagelschmidt gives a summary of eosin literature in so far as it concerns biology and therapeutics.

Stimulated by Wassermann's experiments, Thiroloix and Lancien have occupied themselves with the preparation and tests of suitable preparations of selenium. They state that for a man aged 39, suffering from epithelioma of the tongue with metastases, they used a colloid preparation of selenium, which they name "Selenium A". The details of its chemical composition and properties are not known to me. By means of this preparation they brought about a diminution of the glandular swelling and an improvement in the movement of

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Wassermann, Keysser, Berliner klinische Wochenschrift 1912,  
No. 1, p. 4.

Nagelschmidt, Berliner klinische Wochenschrift 1912, No. 3, p. 118.  
Thiroloix-Lancien, Bulletins et mémoires de la société médicale  
des hôpitaux 1912, Vol. 28, p. 197.

Kessler, Semaine médicale 1912, No. 13, p. 150.

v. Oefele. New Yorker medizinische Monatsschrift 1912, No. 5.

the tongue and in the dysphagia; the only unpleasant secondary effect observed after the injections was an attack of shivering. After 5 weeks of treatment by selenium, the diseased glands suddenly became intensely swollen and on puncture a sterile fluid containing selenium escaped. Later the metastases disappeared. In spite of this, the authors are uncertain whether or not their colloid selenium has a prospect of attaining to practical importance.

According to v. Oefele, the defective metabolism in carcinomata is due to insufficient oxidation of sulphur in the organism. This oxidation might, he states, be raised by selenium preparations, wherefore they should be specially considered in the treatment of carcinoma. Kessler also found that in cancer the excretion of sulphuric acid in the urine was considerably diminished, and he therefore tried selenium oxide in the assumption that selenium conveys oxygen to the sulphur. In a case of recurrent carcinoma of the liver, he administered 0.001 gramm ( $\frac{1}{64}$  grain) of selenium oxide 3 times a day, and in a short time observed an increase in body-weight simultaneously with a decrease in the liver dulness. No recurrence occurred in the course of a year. Certainly the author brought forward no proofs that the case described was one of cancer. The treatment by selenium, which the author carried out with selenium oxide and other soluble compounds of selenium in other cases also, is according to him, specially indicated in inoperable and recurrent cases. It consists in the internal administration of 3 to 4 doses a day of a suitable preparation of selenium. It is best to begin with single doses of 0.001 gramm ( $\frac{1}{64}$  grain), which may be gradually and carefully increased.

Ch. E. Walker has prepared a colloid selenium which is said to be less toxic than Wassermann's eosin-selenium. However, it displayed no action in mouse-tumours.

### Ergot of Rye.

A large number of preparations are mentioned in the literature which are prepared from ergot and which have been recommended as substitutes for ergot in therapy; but so far not one of these preparations has performed what was promised.

for it, and not one has been generally recognised. A few years ago G. Barger and H. H. Dale found two substances in ergot, viz., ergotoxin and p-oxyphenyl-ethylamine, which are said to represent the active principles of ergot. Ergotoxin,  $C_{35}H_{41}O_6N_5$ , which is identical with the hydro-ergotinin of Kraft, gives rise to increased blood pressure and contraction of the uterus and is the specifically acting constituent of various preparations, such as sphacelinic acid and sphacelotoxin. Only a small amount is present in the aqueous extract of ergot, as it is almost insoluble in water; it cannot therefore at present be regarded as a substitute for the galenical preparations of ergot (extracts) used hitherto. On the other hand, oxy-phenyl-ethylamine, which is soluble in water, or its chloride, appears to be gaining ground in therapy. It is on the market under the name of tyramin, uteramin, and systogen. J. Burmann has reported upon the preparation of the drug.

p-Oxyphenyl-ethylamine,  $OH \cdot C_6H_4 \cdot CH_2CH_2NH_2$ , a base which was obtained by Schmitt and Nasse in 1865 by heating tyrosin to  $270^{\circ}C.$ , forms white crystals, which can be sublimed and melt at  $160^{\circ}C.$ ; they are only slightly soluble in cold water (giving a strongly alkaline reaction). The hydrochloride,  $OH \cdot C_6H_4 \cdot CH_2 \cdot CH_2 \cdot NH_2 \cdot HCl$ , is readily soluble in water and in alcohol.

According to Barger and Dale, p-oxyphenyl-ethylamine causes a rise of blood pressure and contraction of the uterus. It forms the active principle of the aqueous extracts of ergot and is similar to adrenalin in its chemical and physiological characters\*).

With regard to its therapeutic employment, D. M. Hoyt reports upon tyramin and E. Heimann upon systogen and uteramin. The internal administration of 0.01 to 0.1 gramme ( $\frac{1}{6}$ — $\frac{1}{2}$  grains) to human beings did not, according to Hoyt, affect the blood pressure. On subcutaneous injection, a dose of 0.03 gramme ( $\frac{1}{2}$  grain) of tyramin effected a transient but considerable rise of blood pressure. According to this, the

Barger - Dale, Biochemical Journal 1907, II., p. 240. — Archiv für experimentelle Pathologie 1909, Vol. 61, p. 113.

Burmann, Schweizer Wochenschrift für Chemie und Pharmazie 1912, No. 6, p. 85. — Apotheker-Zeitung 1912, No. 15, p. 138.

\*) Adrenalin formula:  $C_6H_5(OH)_2 \cdot CH \cdot OH - CH_2 \cdot NH \cdot CH_3$ .

Hoyt, American Journal of Medical Sciences 1912, Vol. 144, p. 76.

Heimann, Münchener medizinische Wochenschrift 1912, No. 25, p. 1370.

action is only transient, but may under certain conditions be of service in vaso-motor depression, and in cases of this kind trials appear justifiable. Gastric disturbance need not be feared, but after doses of 0·02—0·04 grammie ( $\frac{1}{3}$ — $\frac{2}{3}$  grain) and the sudden rise of blood pressure which they bring about, retardation of the pulse and irregular cardiac action sometimes occur.

According to Heimann, systogen constitutes a perfect substitute for ergot. It is entirely non-toxic, its dosage can be regulated and it is very efficacious. Involution of the uterus is effected more energetically and in a shorter time after the subcutaneous injection of the drug than by the use of ergot, without causing troublesome symptoms, such as severe after-pains. The author obtained equally good results in retention of membranes after labour. The drug has also proved useful in cases of evacuation of abortion and of curettage. Before Cæsarian section, the author injected 1 c. c. of systogen (0·2 p. c. solution); in retention of membranes 0·5 c. c. subcutaneously 3 times a day (2 days in succession), or 0·5 to 1 c. c. by mouth. The internal medication also furnished a good result in a case of protracted menses. 0·5 grammie was administered 3 times a day 2 days before the commencement and on the first day of menstruation. The bleeding which usually continued for 10 days, was shortened by 3 days and the loss of blood was somewhat diminished, while no troubles arose.

The value of oxyphenyl-ethylamine as a perfect substitute for ergot, as it was stated to be in the communications of Burmann and Heimann, is questioned by Barger and Dale and by M. Guggenheim. According to these observers, the action of ergot, as also stated by Kutscher and Engeland, is due to the combined action of various constituents of ergot and not to the action of a single substance. Besides oxyphenyl-ethylamine, various other proteinogenous amines come into consideration, for example  $\beta$ -imidazolyl-ethylamine, agmatin, isoamylamine and phenyl-ethylamine.

Burmann, Schweizer Rundschau für Medizin 1912, p. 673.

Barger-Dale, Schweizer Wochenschrift für Chemie und Pharmazie 1912, p. 187.

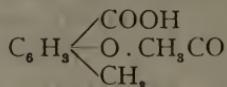
Guggenheim, Therapeutische Monatshefte 1912, No. 11, p. 795.

Kutscher-Engeland, Zentralblatt für Physiologie 1910, p. 479, 589 and 163.

**Ervasin.**

Acetyl-para-cresotic acid (ervasin), a homologue of acetyl-salicylic acid, according to E. Rautenberg, forms prismatic crystals, melting at 140—142° C., which dissolve readily in alcohol, ether and chloroform, but are only slightly soluble in water.

Chemical Formula:



According to Rautenberg's experiments, the preparation is in general well tolerated; several of his patients are even said to have taken daily doses of 8 to 12 grammes (120—180 grains) for a prolonged period without symptoms of poisoning. It causes no disturbance of appetite, no vomiting and no buzzing in the ears. Only in two cases did the author observe nausea to follow a daily dose of 5 grammes (75 grains). The tendency to sweating was the same with equal doses of ervasin and aspirin. When daily doses of 4 to 6 grammes (60—90 grains) were given, no injury of the kidneys was observed; only after the administration of 10 grammes (150 grains) a day for 8 to 12 days did slight albuminuria occur, with very little blood in the urine.

The preparation is indicated in acute and subacute articular rheumatism (also in the presence of neuralgic troubles), and in muscular rheumatism. Rautenberg's results were at first highly satisfactory, and only in the treatment of very severe cases did sodium salicylate prove more reliable. Acetyl-cresotic acid, however, proved of use when employed as a temporary substitute for salicylic acid, especially when renal irritation by salicylic acid was apprehended. In mild cases 0.5 grammie ( $7\frac{1}{2}$  grains) is given up to 4 times a day; in severe cases 1 grammie (15 grains) up to 5 times a day.

According to C. Ehrlich, the indications for ervasin are acute and chronic articular and muscular rheumatism, influenza, neuralgia, fever and all other conditions in which salicylic acid is employed. Ervasin-Calcium (the calcium salt of acetyl-cresotic acid), which dissolves readily in water, may be used in place of it. The dosage is the same as for ervasin.

In acute articular rheumatism, Richter obtained favourable results with ervasin. By means of the drug he not only succeeded in gradually reducing the temperature, but kept it permanently low. The effect on temperature usually took place in 1 to 2 hours, and the effect on pain in half to three-quarters of an hour. No unpleasant secondary effects occurred in connection with the stomach, heart, bowels or kidneys, and endocarditis did not occur during treatment by ervasin.

### Ether.

Anæsthesia by means of the open administration of ether has not as yet been generally adopted on account of technical difficulties, such as freezing of the mask. M. v. Brunn therefore draws attention to a process, the so-called gauze-ether method, which is said to be fairly generally used in England. The procedure, which has been described by Ladd and Osgood and by van Kaathoven, is as follows:

The face is covered with 8 to 12 layers of ordinary gauze, i. e., with an ordinary gauze compress, which must be large enough to cover the nose, mouth, chin and cheeks. On to this the ether is slowly dropped. After about a minute, a second equally thick layer of gauze is placed over the first, and the ether is allowed to drop rather more rapidly on to it. In this way anaesthesia is effected in a short time, without any sensation of suffocation. The thickness of the gauze layer makes it possible, according to the author, to take individual circumstances into account, besides regulating the number of drops. For women and children a thinner layer of gauze may be used.

The author has caused this process to be tried during the last eighteen months in the Tübingen University clinic (for adults combined with scopolamine-omnipon injections). Perthes also has found it useful, especially for operations on the brain. For if an aseptic assistant drops the ether from a

Richter, Berliner klinische Wochenschrift 1912, No. 38, p. 1807.

v. Brunn, Münchener medizinische Wochenschrift 1912, No. 17, p. 920.

Ladd-Osgood, Annals of Surgery 1907, II, p. 460. Zentralblatt für Chirurgie 1907, p. 1491.

Kaathoven, Zentralblatt für Chirurgie 1908, p. 1459.

Perthes, communicated by v. Brunn.

sterile drop-bottle on to a sterile gauze compress, which lies over the covering towel, he finds that ideal asepsis is maintained, while the operator is not annoyed by a mask.

Apart from the fact that anaesthesia is rapidly induced by this method, it offers the additional advantage that the concentration of the ether and air mixture can at any time be altered within certain limits, without apprehension of giving an overdose. Further, the troublesome freezing can readily be avoided by distributing the ether evenly over the entire large piece of gauze, so that even the lowest layers do not become damp and cold, and the narcotic is somewhat warmed before entering the respiratory passages. Von Brunn sums up his opinion of the gauze method by stating that it represents a simple procedure which can be universally employed, and which is as valuable as the method of disinfection by means of tincture of iodine.

Burkhardt's suggestion of producing anaesthesia by means of intravenous injections of ether induced M. Descarpentries to try intramuscular injections of ether, as by this method thrombosis could be avoided\*). He found intramuscular injections of ether especially useful for operations on the face, mouth and respiratory tract. The dosage must vary according to the individual. As a general rule, he proposes to use 1 gramme of ether for every kilogramme of body-weight; it is best applied in the gluteal region according to requirement, in small amounts and at definite intervals. E. Lay advocates this method, because in two cases he obtained satisfactory anaesthesia without complications, while Dumont does not especially recommend it.

Snitowski repeated a method of treating tuberculosis, inaugurated years ago by Wnukoff. It consists in causing the patients to inhale every 2 to 3 hours, by means of an

Burkhardt, Merck's Reports 1909, p. 96, 1910, p. 78, 1911, p. 231.  
Descarpentries, Semaine médicale 1912, No. 18, p. 206. Revue internationale de médecine 1912, No. 15, p. 268. Nouveaux remèdes 1912, No. 12, p. 277.

\*) Compare N. Beresnegowsky, v. Langenbecks Archiv, Vol. 99, No. 1.

Lay, Policlinico 1912, p. 24.

Dumont, Revue de thérapeutique 1912, p. 632.

Snitowski, Semaine médicale 1912, No. 10, p. 116.

atomizer, a mixture of equal volumes of ether and petroleum, to each 150 grammes of which 0·5 to 1 gramme of menthol was added. Wnukoff at the same time injected a solution of 0·3 gramme of menthol in 5 grammes of ether and 95 grammes of castor oil. Snitowski confined himself to inhalations and was able to confirm Wnukoff's observations, namely that as a result of this treatment the temperature returned to normal, while the appetite and vigour were increased. On the other hand, the tubercle bacilli only disappeared from the sputum in one case. The treatment gave rise to no injurious secondary effects.

### Ethyl Chloride.

Ethyl chloride anaesthesia and its significance in practice is discussed by Baumann, A. Stieda and P. Zander. Stieda and Zander recommend the employment of ethyl chloride for inhalation anaesthesia, up to the stage of analgesia, as a practical method of producing anaesthesia, suitable for the general practitioner. The method of employing the preparation is very simple. Several loose layers of gauze are placed over the mouth and nose of the patient and the anaesthetic is allowed to drop rather slowly on to it in the neighbourhood of the nose (10 to 20 drops in 10 seconds). On an average 20 to 40 drops for children and women, and 40 to 80 drops for men are usually required in order to produce the desired condition of analgesia. No assistance is required, and the patient need not be placed in any definite position, nor be fastened down in any way. He may even be anaesthetised in a sitting posture. Anaesthesia is produced very rapidly, and on awaking, the patient is immediately ready to get up and go away. When correctly employed, ethyl chloride is free from danger, is readily inspired and causes no suffocating sensation. It is important, however, that no closed mask be used. The method is especially suitable for minor operations. The advantages of ethyl chloride anaesthesia are fully confirmed by Baumann and Neumann-Kneucker.

Baumann, Münchener medizinische Wochenschrift 1912, No. 17,  
p. 922.

Zander, Münchener medizinische Wochenschrift 1912, No. 2, p. 112.  
Stieda-Zander, Medizinische Klinik 1912, No. 12, p. 479.

E. Borchers published a contribution on the technique of ethyl chloride anaesthesia. For open anaesthesia, he recommends that the ethyl chloride be supplied in tubes with a so-called instantaneous stopper, which makes it practicable to apply the drops at the desired rate. The author has used ethyl chloride for the total enucleation of the tonsils with highly satisfactory results, even in children.

The good results of Braun's mandibular anaesthesia by injections of cocaine and suprarenin induced A. Neumann-Kneucker to attempt to bring about preliminary anaesthesia by spraying on ethyl chloride. For short operations, which are not likely to cause complications, for example dental extractions, this procedure is attended with good results, but the instruments must be ready to hand, as anaesthesia is rapidly produced and disappears with equal rapidity. In carrying out the anaesthesia, the area under treatment must be dried with cotton wool, and the ethyl chloride is then sprayed upon the retromolar triangle. One circumstance which militates against initial anaesthesia by means of ethyl chloride is the presence of deep caries with living pulp, or with pulpitis of the last lower molar, especially if its cavity lies distally. In this case, the ethyl chloride on coming in contact with the wisdom tooth may cause pain. But the method has been successfully used for the extraction of all other teeth, even in the presence of pulpitis or of periostitis, and for other small operations on the lower jaw.

### Ethyl Hydrocupreine.

J. Morgenroth has continued his chemo-therapeutic researches with ethyl hydrocupreine\*). In order to improve upon the results obtained in pneumococcic infection, he attempted, on the ground of theoretical considerations, to retard the absorption of the drug. Therefore, instead of using an aqueous solution of ethyl hydrocupreine sulphate, he used

Borchers, Münchener medizinische Wochenschrift 1912, No. 41, p. 2221, No. 50, p. 2736.

Neumann-Kneucker, Medizinische Klinik 1912, No. 17, p. 693. — Österreichische Zeitschrift für Stomatologie 1912, No. 12, p. 375. — Zahnärztliche Rundschau 1912, No. 2, p. 55.

Morgenroth, Berliner klinische Wochenschrift 1912, No. 14, p. 663.

\*) Compare Merck's Report 1911.

oily solutions of the free base. By the prophylactic employment of a 2 p. c. solution in olive oil, he found that 90 to 100 p. c. of infected mice, treated with doses of 0·5 to 0·4 grammes for 4 days, were cured, whereas in his previous experiments with aqueous solutions of the alkaloid, he had only succeeded in curing 50 p. c. By this treatment, a single dose of 0·7 gramme for every 20 grammes of mouse, with simultaneous infection, affords lasting protection. In the author's opinion, several days' treatment may cause immunity processes to occur, which aid in arresting development, and may be of significance for the final effect. He thinks that the simultaneous injection of large doses together with the infection may cause the death of the pneumococci in the peritoneal cavity; but the author does not wish to deny the possible occurrence of more complicated processes.

Even though Morgenroth's results prove that ethyl hydrocupreine exercises a considerable influence on pneumococcic infections of mice, the clinical employment of the preparation in pneumonia is not yet ready for trial. It is even doubtful whether there is any prospect of employing the drug, or whether further researches are necessary in order to find in the group of quinine derivatives, to which ethyl hydrocupreine belongs, one having a more reliable action. The preliminary experiments of A. Fränkel in 21 cases of pneumonia showed no evident action in 43 p. c., a doubtful action in 28·5 p. c. and a marked action in 28·5 p. c. of the cases. Fränkel concludes from his results that ethyl hydrocupreine is not the drug which the physician needs, because it gives rise to unpleasant complications, which, although they only occur in a certain percentage of cases, are of such a nature that it cannot be recommended for practical employment. They consist, according to the author, in the appearance of amblyopia, which he observed in 14 p. c. of his cases. For a single dose 0·5 gramme ( $7\frac{1}{2}$  grains) of ethyl hydrocupreine was given. For a daily dose 1 to 2·5 grammes (15—40 grains) were administered internally. After observing the secondary effects which have been mentioned, Fränkel went back to a daily dose of 1·5 to 2·0 grammes (24—30 grains). Certainly the amblyopia was in every case of a mild degree,

and rapidly disappeared on leaving off the drug, so that in the course of two days the patient's vision again returned to normal. But Fränkel believes that had the medication been continued, severe and perhaps even lasting visual disturbances would have occurred. Further experiments will be required to show whether or not small doses, which do not give rise to amblyopia, are capable of producing satisfactory results. Wright, according to Morgenroth, injected large doses of the preparation subcutaneously, and (in 8 cases) observed no amblyopia.

Like quinine, ethyl hydrocupreine also possesses an anaesthetic action. In experiments on rabbits, Morgenroth and Ginsberg came to the conclusion that the subconjunctival application of sufficiently concentrated aqueous solutions causes total anaesthesia of the cornea. Its duration also is very prolonged. Thus, the 20 p. c. solution produces anaesthesia which is still absolute after 10 days and only disappears after 16 days. A 10 p. c. solution produces complete anaesthesia lasting 4 days, and a 2 p. c. solution produces anaesthesia in 3 minutes, which lasts from 45 minutes to 2 hours. The 10 p. c. oily solution of ethyl hydrocupreine (base) is also a good anaesthetic, but its action is neither so powerful nor so lasting as that of the aqueous solution of the hydrochloride. The more concentrated solutions gave rise to transitory turbidity of the cornea as a secondary effect.

### Eucalyptus Oil.

Eucalyptus oil was recommended about 20 years ago by J. B. Curgenven as a prophylactic and curative for the treatment of scarlet fever, and has probably also been used in the practice of English physicians\*). Curgenven generally used a mixture of eucalyptus oil and other ethereal oils, camphor and menthol, a few drops of which were taken internally shaken up with water and with which the whole body was sponged over. He also believed that dresses, beds and floors could be efficiently disinfected by its use.

Morgenroth-Ginsberg, Berliner klinische Wochenschrift 1912, No. 46, p. 2184.

Curgenven, British Medical Journal 1890, I, p. 723.

\*) Compare Lancet 1911, I, p. 1671.

In recent years R. Milne has further worked out the eucalyptus treatment of scarlet fever and has given special directions for its employment, for which reason his method of treatment is now known as Milne's method. It consists in painting the whole body of the patient with eucalyptus oil. By this measure, according to Milne's experiences, the danger of infection is removed, so that it becomes unnecessary to isolate scarlet fever patients from other patients.

The method was tested by E. Koerber and M. Kretschmer. Koerber came to the conclusion that Milne's eucalyptus treatment is not reliable, as further infection occurred in spite of it. Nor did he find that the duration of the disease was shortened. Some only of the usual complications of scarlet fever remained absent.

Kretschmer also found that Milne's method did not perform all that it promised. As it is said besides not to be very pleasant for the patients, he discarded it.

### Euguform.

This preparation, which was mentioned in my Annual Report for 1901, was recommended at the beginning of the year by Hoffmann for the treatment of foot and mouth disease. The new method of treatment for this troublesome disease of cattle aroused much interest. The treatment consisted in applying euguform to the udder and hoofs. A thin layer of a 10 p. c. euguform ointment was lightly applied to the udders of the cows, whereupon the skin became soft and any scabs and ulcers dried up. The hoofs were syringed with an aqueous suspension of euguform and the animal's mouth was rinsed with it. Besides the treatment by euguform, quinine was administered for the fever and hot compresses were applied; the cowsheds were disinfected with formaldehyde. The results were, according to Hoffmann, quite brilliant. But, apart from the fact that the scientific basis of the new method of treatment was insufficient, further tests gave such poor re-

Milne, A plea for the home treatment and prevention of scarlet fever, 1910. — Lancet 1911, I, p. 1070.

Koerber, Münchener medizinische Wochenschrift 1912, No. 11, p. 581.

Kretschmer, Münchener medizinische Wochenschrift 1912, No. 33, p. 1809.

Hoffmann, Frankfurter Zeitung 1911, 14<sup>th</sup> December.

sults that the hopes aroused by Hoffmann's method remained unrealised\*).

E. Sieburg discusses the pharmacology of euguform. His tests show the former assumption that euguform acts by splitting off formaldehyde to be unproven. On the other hand, after the action of enzymes, the presence of formic acid could be demonstrated, and on feeding dogs with the preparation, it appeared in their urine. On the whole, euguform proved to be a non-poisonous body, with which further tests may be carried out on animals without apprehension. Whether the formic acid which is split off would act injuriously on human beings, the author does not venture to decide.

### Eulatin.

In bronchial affections and influenza, eulatin\*\*) has, according to Hirschberg, proved a useful drug. Its effect was most definite in those forms of bronchitis in which the catarrh was limited to the trachea and the larger bronchi, and in which therefore only sonorous râles were heard. In these cases improvement and a marked diminution of the dry cough were manifest after 1 to 2 days. The action of the drug was less prompt when the catarrh had extended to the finer bronchi, but here also it set in after a few days. In all cases of bronchitis, the duration of the disease could be shortened by the administration of eulatin. The author prescribed 1 tablet (0.25 gramme) (4 grains) 3 to 5 times a day for children, and 2 tablets 4 to 6 times a day for adults. The favourable action of the preparation depends, according to Hirschberg, on the expectorant property of benzoic acid and the antispasmodic property of bromine, to which the action of antipyrine is added. The last named component of eulatin induced the author to try it in influenza, in which it proved successful. Headache, backache, conjunctivitis and irritating cough were favourable influenced in the course of 1 to 2 days; cases in which gastric symptoms predominated were less benefited.

\*) Compare Wille, Berliner tierärztliche Wochenschrift 1912, p. 9 and 32. — Süddeutsche Apotheker-Zeitung 1911, No. 96, p. 771.  
— Apotheker-Zeitung 1912, No. 13, p. 120.

Sieburg, Apotheker-Zeitung 1912, No. 42, p. 385.

\*\*) Compare Merck's Reports 1908—1911.

Hirschberg, Deutsche Medizinal-Zeitung 1912, No. 3, p. 47.

The usefulness of eulatin in whooping-cough is confirmed by U. A. Stheeman, C. A. Cammaert and F. Franke. The last named author reviews the eulatin literature which has appeared up to the present.

### Eumenol Tablets.

Eumenol, on account of its excellent action in menstrual disturbances, has recently aroused so much interest in therapeutics that I have decided to supply the drug in the form of tablets, in order to facilitate its administration.

Eumenol is the fluid extract of the root of a plant of the natural order Umbelliferæ (?) indigenous to China, the species of which has not yet been determined. In its native land the drug, according to F. Hirth, has, under the name of Tangkui or Man-mu, been highly prized for thousands of years as a drug which regulates menstruation.

Some years ago E. Lezenius investigated the question of the origin of Tangkui root. He sought to decide whether the root was obtained from one of the Araliaceæ, or as other authors\*) have stated, from one of the Umbelliferæ, *Levisticum officinale* Koch. On the ground of his anatomical investigations of various roots, the author came to the conclusion that Tangkui root was obtained from one of the Umbelliferæ, which was nearly related to *Levisticum officinale* Koch. He considers that Henry's and Diels' assumption that this member of the Umbelliferæ was *Ligusticum acutilobum* might be true, but he was unable to obtain the root of this Japanese plant and could not therefore adduce any proof of this assumption. The

Stheeman, Nederlandsch Tijdschrift voor Geneeskunde 1912, I., p. 668.

Cammaert, Nederlandsch Tijdschrift voor Geneeskunde 1912, II., p. 15.

Franke, Allgemeine medizinische Zentralzeitung 1912, No. 30, p. 388.

Hirth, Münchener medizinische Wochenschrift 1899, No. 23, p. 769.

Lezenius, Pharmazeutische Zentralhalle 1910, No. 12, p. 221.

\*) Communicated by Lezenius. (Bretschneider, *Botanicon sinicum I—III.* — Ruprecht, [Tartarinow] *Catalogus medicamentorum sinensium*, St. Petersburg 1856. — Gauger, *Repertorium für Pharmazie und praktische Chemie in Russland* 1848, Vol. 7, p. 13. — Hanbury, *Science Papers* 1875, p. 260. — Oliver, *Hookers Icones Plantarum* 1891, Vol. 10, Plate 1999. — Diels, *Englers botanisches Jahrbuch* 1901, Vol. 29, p. 500. — Dragendorff, *Die Arzneipflanzen* 1898, p. 494.)

experiments and analytical investigations carried out with fluid extracts of Tangkui root and of roots of *Levisticum officinale* may be considered to confirm the origin of Tangkui roots from *Levisticum officinale*, or from a nearly related plant.

The earliest therapeutic communications to European literature are found in the eighteenth century\*); but Tangkui was first introduced into therapeutics in 1899, after Heinz had given pharmacological proof of the non-toxicity of the preparation, which had been emphasised by the Chinese, and after A. Müller had placed eumenol treatment on a scientific basis.

Müller tested the action of eumenol in a series of cases, and found it to be a useful tonic which exercises a favourable influence on menstrual processes. In conjunction with the usual methods of treatment, it hastened the commencement of delayed menstruation in most cases, produced the menstrual flow which had remained absent, and alleviated or cured pain, especially pre-menstrual pain. The author fixed the dose of eumenol at one teaspoonful, 3 times a day.

In order to allay any apprehension that eumenol might bring about abortion, reference should be made to Heinz's experiments on animals and Müller's observations on women, which show that the drug does not act injuriously either at the commencement or during the course of pregnancy.

Müller's experiences were fully confirmed by de Buck's investigations. This author also attributes to eumenol a favourable influence on the catamenial functions. According to his researches, it also has a regulating action on the abnormal local and general reactions which accompany the menstrual processes. The best results are obtained with eumenol in purely nervous troubles, which are not connected with any gynaecological lesion. In these cases the dysmenorrhœic symptoms may be completely cured. In other cases, accompanied by organic disease, although the action of eumenol is plainly evident, it can only be looked upon as purely palliative.

H. Langes obtained striking results by the use of eumenol in dysmenorrhœa of nullipara and in severe bleeding.

\*) Compare Lezenius.

Müller-Heinz, Münchener medizinische Wochenschrift 1899, No. 24,  
p. 796.

de Buck, Belgique médicale 1899, No. 48.

Langes, Therapeutische Monatshefte 1901, No. 7, p. 363.

of multipara. Pains in the back and abdomen, which were wont to occur during the first days of menstruation, disappeared immediately on the prophylactic employment of eumenol. They re-appeared after 3 months, but were again favourably affected by the use of eumenol. Even in a case of chronic endometritis with salpingitis and oöphoritis the profuse haemorrhages were stopped in a short time by the administration of 300 grammes (10 oz) of eumenol, while their recurrence was regulated. The symptoms caused by moderate retroversion were improved and the haemorrhages during pregnancy were alleviated. The author prescribed eumenol during the week preceding the menses — one tablespoonful to be given 3 times a day before meals. The total amount administered during menstruation amounted to 100 to 150 grammes ( $3\frac{1}{3}$ —5 oz).

While Müller recommends massage and hydrotherapy besides eumenol medication, R. Palm refers the success achieved by him in the treatment of amenorrhœa by eumenol solely to the use of the preparation, as he had resorted to no other measures. The author has used the drug in his practice for nine years and expresses himself well satisfied with its action.

The active principle of eumenol has not as yet been determined nor investigated in detail. Bufalini, who investigated eumenol in this direction, was unable to discover either an alkaloid or a glucoside and therefore assumes that the action of Tangkui root is due to the presence of essential oils (resins), for the aqueous distillate of the extract displays a feebly sedative action on frogs. Its action is certainly in part due to tannin.

As eumenol possesses a pronounced, characteristic taste, which according to Palm and other physicians, is repugnant to many patients, the eumenol tablets prepared by me should prove a welcome form of administration in these cases.

### Ferrosajodin.

Ferrosajodin in the form of tablets (1 tablet corresponds to 0.12 gramme [2 grains] of iodine and 0.03 gramme [ $\frac{1}{2}$  grain] of iron) was tried by G. Brühl in the place of syrup of ferruginous iodide for scrofulous and anaemic children, and he was

Palm, Münchener medizinische Wochenschrift 1910, No. 1, p. 23.

Bufalini, Annali di farmacologia 1900, p. 140.

Brühl, Therapie der Gegenwart 1912, No. 6, p. 286.

well satisfied with the results. During the first week of treatment he prescribed one tablet after lunch, during the second week two tablets, and during the third week three tablets after meals. He continued the last named dose for months. The result of this medication was that the children usually looked better and more alert, the appetite was improved and they gained in weight. Slight glandular enlargement, such as often occurs simultaneously with hypertrophy of the lymphatic tissue of the throat, decreased in size or disappeared. Especially after the removal of enlarged tonsils and adenoids, sajodin proved useful in causing the disappearance of the symptoms.

The experiments with ferrosajodin on children between the ages of 6 and 15, which were carried out by Dierbach, confirm Brühl's results.

### Fibrolysin.

W. Böttcher tried the effect of fibrolysin treatment in a case of carcinoma brought about by the frequent application of X rays. He injected the contents of one ampoule of fibrolysin alternately into the left and right lumbar region every second day. The treatment was not found by the patient to be particularly painful and was well tolerated. The appetite was improved. The first injections caused no evident changes, either in the ulcer or in the cutaneous scar tissue. After a few further injections, there appeared at the base of the ulcer, which had been well cleansed by hydrogen peroxide solution and was covered with red warty vegetations, several points of a dirty grey colour. These represented necrotic areas of tissue and were partly loosened by the removal of the dressing, and in part, as a result of irrigation with hydrogen peroxide solution, hung in larger or smaller fragments. At the same time there was evidence of distinct softening of the cutaneous scar tissue. Suspicious accessory circumstances showed the diagnosis to be one of true carcinoma, wherefore an operation was performed with a successful issue. The author considers the favourable result to be in part due to treatment by fibrolysin, by means of which the scar tissue was softened and the blood supply consequently improved,

thus rendering the conditions more favourable for healing. Since the fibrolysin treatment was continued until shortly before the operation, the action of the drug was extended to the process of healing after the operation, as the author was able to recognise by the appearance of the scar tissue. He therefore considers that before undertaking an operation on extended or contracted cutaneous scar tissue, a prolonged course of fibrolysin injections is advisable.

Further communications on the value of fibrolysin in scars, adhesions and contractions have been made by H. Sgobbo, Depage and Froehlich, W. Falgowski, J. Zilz, M. Fränkel, Fellenberg, Huitfeld, L. Marchetti, F. Mendel and A. Osti.

Sgobbo obtained good results with fibrolysin, not only in recent but also in old scar tissue. It is more efficacious when injected in the neighbourhood of the diseased area.

Depage and Froehlich confirm the action of fibrolysin in cicatrized oesophageal strictures, and Falgowski confirms the value of the drug in cicatrices consequent upon inflammatory diseases of the adnexa, including parametritis and perimetritis, especially when used in combination with vibratory massage.

Zilz treated the cicatrices remaining after fractures of the jaw with fibrolysin, in order that the cosmetic result might be as good as possible. The scars were cleansed with ether and benzine, after which fibrolysin plaster was applied and changed every 24 hours. This treatment was adopted during the last week of residence in hospital and was markedly efficacious in softening the scar tissue.

Fränkel, referring to 9 cases treated by himself, points out the favourable influence of fibrolysin injections on multiple scleroses; they not uncommonly lead to remissions and im-

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Sgobbo, Zeitschrift für Ohrenheilkunde etc. 1912, Vol. 66, No. 1 and 2.

Depage-Froehlich, Journal médical de Bruxelles 1912, No. 47.

Falgowski, Gynäkologische Rundschau 1912, No. 9.

Zilz, Österreichische Zeitschrift für Stomatologie 1912, No. 4.

Fränkel, Neurologisches Zentralblatt 1912, No. 20.

Fellenberg, Schweizer Rundschau für Medizin 1912, No. 5.

Huitfeld, Norsk Magazin for Laegevidenskaben 1912, No. 6.

Marchetti, Rivista medica 1912, April.

Mendel, Deutsche Zeitschrift für Chirurgie 1912, Vol. 113.

Osti, Zentralblatt der experimentellen Medizin 1912, Vol. 2, No. 6.

provements. They are only contra-indicated in cases with a very acute onset.

Fellenberg describes a case of uterine adhesions, in which the uterus was so generally adherent and immovable that advancing pregnancy gave rise to severe pain. Before inducing abortion, the author tried the effect of fibrolysin. The result was highly satisfactory, for the adhesions broke down, the pain disappeared, and labour took place normally and without complications.

Marchetti prescribed fibrolysin in a case of urethral stricture which had defied all mechanical measures, with the result that the introduction of the sound was facilitated even after the first injection. The difficulty experienced in voiding urine disappeared. The improvement effected after 10 injections was not lasting, but a second series of injections led to a permanent result; the patient experienced no return of the trouble, even after 3 years.

Huitfeld reports two cases of contraction of the fingers, in which fibrolysin proved of value. One case is of special interest, because the desired result was obtained in the same time as would have been the case after operation. The infiltrations present on the surface of the hand were enlarged after the first injection, the itching and burning which had been felt previously in the contraction were augmented and in time the subjective troubles disappeared. After 7 injections the contracted finger could be extended without much pain.

Mendel disputes the adverse opinion of Sidorenko, which this author\*) held on account of a few failures with fibrolysin. He justly draws his attention to the large number of undoubtedly successes which many different observers have obtained with the preparation\*\*). In order to draw up a critical review of the results of treatment with fibrolysin, he separates the affections treated by the drug into three groups. Firstly, there are the cases in which spontaneous healing is possible and in which therefore the positive results of fibrolysin treatment cannot be established with mathematical precision. Further, there are cases in which the simultaneous employment of mechanical, hydropathic and electric measures only leads to improvement after the employment of fibrolysin has been

\*) Sidorenko, Merck's Report 1911, p. 244.

\*\*) Compare Merck's Reports 1904—1911.

begun. Finally, there are certain affections which never heal spontaneously and are never healed or improved by other methods, with the exception of surgical procedures. But in this class a large number of cures may be guaranteed by fibrolysin treatment. Thus, if in the first two categories of diseases the value of fibrolysin should be doubted, the cases belonging to the third category, which were formerly considered incurable, afford absolute proof that in fibrolysin we possess a drug which has a specific action on scar tissue, leading to a cure.

Osti shows in a paper how the action of fibrolysin in indurative pneumonia may be explained. According to him, the employment of fibrolysin causes the appearance of proteolytic ferments in the blood, like those occurring during the normal crisis of pneumonia. These are the result of the action of fibrolysin in stimulating leucocytosis. They liquefy the fibrin of the exudate, while the cells of the exudate undergo fatty degeneration, and being dissolved by the steatolytic ferment of the lymphocytes, can be absorbed. The practical aspect is illuminated by a case of contracted lung reported by W. Stoeltzner, a disease well known to be little affected by treatment. The case was one of a boy aged 7, who as a result of pneumonia was suffering from distinct contraction of the right half of the thorax with curvature of the spine. In the course of 3 weeks the contents of 10 ampoules of fibrolysin were injected subcutaneously between the shoulder blades. During this time the fever subsided and the boy gained in weight. On examination after 4 weeks, the dulness and bronchial breathing, as well as the contraction, were found to have totally disappeared. This result calls for the employment of fibrolysin in similar cases.

A typical case of epigastric hernia is described by S. Wygodzinski. Treatment consisted in rest cure, mixed diet and fibrolysin injections. The injections were given on alternate days in doses of 2-3 c. c. (= 1 ampoule) subcutaneously in the neighbourhood of the hernia. After the injection, which was carried out under aseptic precautions, the author had the area of injection carefully massaged for some time. He gave 20 injections in all. In 6 weeks the hernia had disappeared. This result was obtained exclusively by means of fibrolysin.

A further indication for the employment of fibrolysin is afforded, according to K. Tietze, by salvarsan infiltrations, which may occur as a consequence of intra-gluteal injections of salvarsan. In order to avoid operative procedure, e. g., the separation of the necrotic tissue, injections of fibrolysin may be tried; by this means the author succeeded in bringing about the softening of hard infiltrations, which had persisted for months.

R. del Valle y Aldabaldé has supplied a contribution to the fibrolysin treatment of chronic rheumatic joint diseases. It is of special use when other methods of treatment have proved unsuccessful and when the disease is fibrotic in nature. As soon as the acute symptoms have subsided, an intramuscular injection may be given every second day. When a tendency to haemorrhage exists, fibrolysin is contra-indicated under all circumstances, and arterio-sclerosis and cerebral arterio-sclerosis form a relative contra-indication.

In the ankylosing forms of gonorrhœal rheumatism, which are refractory to ordinary treatment, L. Benasson recommends the employment of fibrolysin injections combined with massage. The use of this treatment has given rise to excellent results.

Fibrolysin treatment also deserves consideration in arthritis. Thus, in a case of chronic gout, Friedberg used fibrolysin in the form of injections. After 15 injections, he observed the tophi to grow softer and the joints of the fingers and hands became more movable. After 5 further injections, the patient had improved so much that he could be treated by massage. K. W. Spatow was able to confirm the favourable influence of fibrolysin injections in arthritis deformans.

The communications of P. Cohn, Vandoren, von Marenholtz and Rusche are of interest in ophthalmology.

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Tietze, Dermatologisches Zentralblatt 1912, Vol. 15, No. 5.  
del Valle, Revista de medicina y cirujia practicas de Madrid 1911,  
Vol. 35, No. 1199.

Benasson, Thèse de Paris 1911.

Friedberg, Fortschritte der Medizin 1912, No. 18.

Spatow, Wratschebnaja Gazeta 1912, No. 35—36.

Cohn, Wochenschrift für Therapie und Hygiene des Auges 1912,  
Vol. 15, p. 277.

Vandoren, Archives médicales belges 1912, August.

Marenholtz, Zeitschrift für Augenheilkunde, Vol. 28, No. 6.

Rusche, Deutsche medizinische Wochenschrift 1912, No. 3, p. 144.

Cohn attempted to remove strictures of the lachrymal duct by the use of instillations of fibrolysin, but when he had convinced himself of the futility of this procedure, he passed to the following method of treatment. By means of a fine, bent platino-iridium cannula he introduced about 1 grammé of a fibrolysin solution, to which a little 2 p. c. cocaine solution had been added, by way of the inferior lachrymal duct, which had been slightly slit up, to the stenosed part, withdrawing the cannula the moment he noticed the fluid pass. Thus he achieved the complete irrigation of the constricted part. During this treatment, care should be taken by timely drawing up of the chin to avoid the penetration of the evil-tasting solution into the buccal cavity. By this method of treatment the author obtained excellent results in a number of cases, and was thus able to confirm the results described by Grossmann and Cauvin of fibrolysin treatment of epiphora. As the method is free from danger, practically painless and can be carried out without much difficulty, and at the same time ensures a successful issue, it deserves the consideration of the oculist.

In a case of symblepharon, caused by burning of the conjunctiva by a red-hot iron, Rusche injected fibrolysin directly into the scar. After 6 injections, the movement of the eye-ball had improved and the scar was moderately stretched. In a case of cervix bulbi with extensive cicatrical changes of the upper and lower lids, in which contraction of the lids and conjunctiva made it impossible to separate the upper lid from the surface of the eye-ball, and the conjunctiva was tightly stretched, fibrolysin (0.1 to 0.2 c. c.) was applied to the cicatrices and the conjunctiva, and at the same time milk compresses were applied. After 10 injections the lids could be raised and the xerosis of the cornea had so far improved that the patient could see better. The results of fibrolysin treatment are, according to the author, less satisfactory in corneal opacities, in scrofulous, purulent and trachomatous keratitis, in chronic uveitis and in retrobulbar neuritis, and also on the whole in exudation into the vitreous humour and into the posterior segment of the eye-ball.

In a case of traumatic cicatrisation of the eye, which gave rise to double vision and retraction of the upper lid, Vandoren

Grossmann, Merck's Report 1909, p. 206.

Cauvin, La clinique ophtalmologique 1910, October.

injected 2 c.c. of fibrolysin every 3 days, and applied hot fomentations twice a day. He obtained a surprisingly good result. He was no less successful with this treatment in a case of almost total blindness caused by turbidity of the vitreous, and in a case of ectropion of the lower lid following erysipelas. In chronic leucoma and in parenchymatous keratitis, fibrolysin was less beneficial, and in old exudations of the iris its employment was unsuccessful.

In a case of pemphigus of the conjunctiva, in which wing-like granulations were beginning to form, von Marenholtz tried to save the eye by means of instillations of fibrolysin. After its daily application for 4 months, he had at least prevented the granulations from extending in a horizontal direction, while they had decreased considerably in thickness and had become more transparent.

In a case of quinine blindness, which had been caused by taking too large doses of quinine by mistake, fibrolysin, according to Kulebjakin, proved of value. A case of fibrolysin idiosyncrasy, reported by Santíñá, deserves mention. It must have been due to idiosyncrasy, as the author met with no similar symptoms among the other patients he was treating with fibrolysin. The symptoms consisted of a rash and of swelling of the face and scrotum during treatment by intramuscular fibrolysin injections in a case of adhesive otitis media. Another case of pronounced idiosyncrasy is described by F. Brandenberg. This patient always reacted to fibrolysin injections by rigor, rise of temperature and rapid pulse, symptoms which disappeared in 8 hours; there was no demonstrable seat of disease and there were no local symptoms of irritation.

Interesting communications have also been made regarding the use of fibrolysin in veterinary practice. Th. Seibert used fibrolysin with complete success in a race-horse, which, as the result of a fall, had contracted a thickening of a tendon on the fore-foot and walked lame. The animal was given an

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Kulebjakin, Medizinische Klinik 1912, No. 28, p. 1169. — Westnik Ophtalmologii 1911, No. 1.

Santíñá, Revista Barcelonesa de enfermedades de oido etc. 1911, Vol. 7, No. 26.

Brandenberg, Fortschritte der Medizin 1912, No. 38, p. 1186.

Seibert, Münchener tierärztliche Wochenschrift 1912, No. 1.

injection of 11.5 c. c. of fibrolysin into the left side of the neck every 3 days, which led to marked improvement in a comparatively short time. After the administration of 5 injections, the horse was so far cured that it could return to work. An examination after 7 months showed that the tendon had become soft and supple and that the animal moved perfectly in all forms of gait. Leicht obtained similar results in a horse, in which the tendinous thickening was so great that the circumference of the affected leg was double the normal size. In the course of 10 days 5 injections were given into the neck. Thereupon the thickening diminished and after 3 weeks had disappeared, except for a slight thickening around the site of puncture. The lameness was also cured.

R. Reichenbach tried fibrolysin in a case of thrombosis of the femoral artery. The diseased horse, which always went lame after a short time, was given 10 c. c. of fibrolysin intravenously, after which it showed only slight lameness, even after arduous work. After a second injection, the trouble entirely disappeared.

Fibrolysin was also administered with success by: Luginger in a horse with painful thickening of the hind foot, Ponader in extensive malanders, Gerasimow in inflammation of the tendons of the fore-feet of a horse, N. Wolkow in lameness, tumours and neglected elephantiasis of horses, P. Kosekin in chronic parenchymatous inflammation of the cornea, and H. Lindenberg in a series of cases comprising lameness, thickening of the fetlock and hock, hard callus resulting from fracture of bones, chronic tumour of the ankle, and chronic inflammations of the tendons in the legs in horses.

Finally, attention may be drawn to a work by S. Peller, in which he points out the utility of fibrolysin in removing tattoo marks.

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Leicht, Münchener tierärztliche Wochenschrift 1912, No. 23.  
Reichenbach, Berliner tierärztliche Wochenschrift 1912, No. 13.  
Luginger, Münchener tierärztliche Wochenschrift 1912, No. 16.  
Ponader, Münchener tierärztliche Wochenschrift 1912, No. 32.  
Gerasimow, Veterinarny Wratsch 1912, No. 16.  
Wolkow, Veterinarny Wratsch 1912, No. 4.  
Kosekin, Veterinarny Wratsch 1912, No. 20.  
Lindenberg, Veterinarny Wratsch 1912, No. 15.  
Peller, Dermatologische Zeitschrift 1912, Vol. 19, No. 10, p. 900.

**Filmaron.**

L. Mendelsohn gives the following instructions for the cure of tapeworm by filmaron\*). On the day preceding treatment very little food is given and in the evening older children and adults are given herring salad containing plenty of salt and onions. For young children limitation of diet is sufficient. Next morning the filmaron oil is taken on an empty stomach. Adults are given 10 grammes of filmaron oil (1 gramme of filmaron), children 5 to 7.5 grammes. Smaller doses may jeopardise the result; on the other hand adults may receive 15 grammes of filmaron oil without apprehension. If the bowels are not opened one hour after the medication, one tablespoonful of castor oil is given, which may be repeated again if necessary. Filmaron oil is, as a rule, taken willingly even by children and is well tolerated. The results of the filmaron cure were, according to Mendelsohn, very satisfactory. In 11 out of 12 cases the worm was finally expelled. In agreement with other writers, the author therefore declares filmaron oil to be an innocuous drug, easy to take and very efficacious, and, especially in practice among children, superior to the preparations customarily used hitherto. H. Buch and Ardell arrived at similar results.

**Fuchsine.**

The ordinary commercial fuchsine is the chloride, the sulphate or the acetate of rosaniline and para-rosaniline. Rosaniline acetate (+ para-rosaniline) is also known as rosein or basic fuchsine. It usually consists of irregular, glittering green fragments, which dissolve readily in water and alcohol. This preparation, according to E. S. May, is said to possess a pronounced bactericidal action, which in some respects is even superior to carbolic acid. It is also said, like the well known scarlet-red, to promote the formation of epithelium and of granulation.

Mendelsohn, Berliner klinische Wochenschrift 1912, No. 32.

\*) Compare Merck's Reports 1903—1907 and 1910.

Buch, Finska Läkaresällskapets Handlingar 1912, No. 54.

Ardell, Allmäna Svenska Läkartidningen, Pharmazeutische Zeitung 1912, No. 1, p. 8.

May, Journal of the American Medical Association 1912, Vol. 58, No. 16, p. 1174.

The germicidal action of organic dyes is not new; I need only refer to the works of Penzoldt. But the theory of the action of fuchsine acetate, advanced in the Journal of the American Medical Association\*), is new and original. It may be impartially summarised as follows: Fuchsine acetate behaves in solution as a base, for in aqueous solution it is decomposed into rosaniline (tri-p-amido-m-tolyl-diphenyl-carbidride) and acetic acid, but the former is more strongly basic than the latter is acid. The exact opposite is the case with the chloride and sulphate of rosaniline. Therefore an aqueous solution of fuchsine acetate reacts as though it contained the free base. But the free base is known to be unstable; by the interchange of the molecules, it is transformed into a colourless derivative having the same composition but a different structure. Acids effect the opposite process and reproduce the dye. In a solution of fuchsine acetate, this would signify a continual change in molecular structure, and these alterations would necessitate the wandering of electrons from one position to another. Thus it is conceivable that this wandering of electrons and the resulting energy form the cause of the bactericidal action.

It is impossible to say whether, on account of the above explanation, fuchsine acetate should in practice be considered superior to the other rosaniline salts. Triboulet does not fix the kind of fuchsine for his method of treatment. In various skin diseases, such as impetigo and pyodermitis, he used Ziehl's carbol-fuchsine, a solution of 1 grammé of fuchsine and 5 grammes of carbolic acid in 10 grammes of alcohol and 90 grammes of water. He applied this by means of swabs to the crusts which had been previously softened by a 0.08 p. c. zinc sulphate solution. He states that the solution dries up, forming a varnish which protects the cutaneous areas from the access of air. The eruptions dry up and after several days of treatment the crusts can readily be removed, whereupon the scars soon heal.

Penzoldt, Archiv für experimentelle Pathologie 1890, Vol. 26, p. 310.

\*) Journal of the American Medical Association 1912, Vol. 58, No. 19, p. 1465. — Cleveland Medical Journal 1912, June.

Triboulet, Klinisch-therapeutische Wochenschrift 1912, No. 43, p. 1276.

I. Guareschi suggests a new test for bromine, the chief component of which is fuchsine. It consists of filter paper soaked in decolourised 1 p. c. fuchsine solution (fuchsine sulphurous acid.) It is reddened by bromine vapour and remains unchanged on contact with iodine, chlorine and chromoxychlorides. To carry out the test, a little solution of chlorine is added to the solution of the halogen salt or salt mixture to be tested and the fuchsine paper is suspended over it. The commencement of the reaction can be hastened by gently warming.

In place of the fuchsine sulphurous acid, according to Denigès and Chelle, a solution of fuchsine in dilute sulphuric acid may be used. This reagent is prepared by mixing 10 c. c. of a 0·1 p. c. solution of fuchsine and 100 c. c. of 5 vol. p. c. sulphuric acid and leaving it to stand until it has become colourless. This occurs in about an hour. Then 25 c. c. of this reagent are mixed with 25 c. c. of pure acetic acid and 1 c. c. of sulphuric acid. One drop or more of the fluid to be tested for chlorine, or bromine, is mixed with 5 c. c. of the above mixture. If chlorine is present the mixture turns yellow; if bromine is present it assumes a reddish-violet colour. The reaction is rendered more sensitive if the solution is shaken up with a little chloroform, which takes up the yellow or the red dye.

### Fumiform.

Years ago H. Floer reported upon this preparation, which consists principally of asphalt in the form of tablets. In a recent communication he confirms its favourable influence upon pulmonary tuberculosis. Fumiform is used for fumigation, and the treatment consists in the patients remaining for a definite period every day in a room in which the fumigation is carried out. In the first place the author refers to the cases treated and described by him years ago and states that out of 8 cases 5 remained well. Then he accepts the opinion of over fifty medical men, who acknowledged that the inhalation of fumiform vapour facilitates expectoration, alleviates the cough and

Guareschi, Atti della reale accademia delle scienze di Torino,  
Vol. 47, Chemisches Zentralblatt 1912, II., p. 635.

Denigès-Chelle, Comptes rendus de l'académie des sciences 1912,  
Vol. 155, p. 1010.

Floer, Therapie der Gegenwart 1912, No. 543. — Compare Merck's  
Report 1909, p. 214.

usually also improves the general health\*). Besides the clinical experiences, the author refers to the investigations of Aufrech, which have shown that fumiform fumes kill bacterial cultures (staphylococci and tubercle bacilli, but not the spores of *Bacillus subtilis*), after acting upon them for 10 to 15 minutes.

### Glycerin.

In an investigation of the bactericidal action of glycerin, Gosio found that a mixture of glycerin and water displayed a fatal effect on cholera vibrios. Further investigations will show whether this discovery is of therapeutic value. Glycerin has already been used in the form of enemata in cholera, as the author also points out.

F. Dörken reports on the use of alcohol-glycerin for moist compresses. As among the substances used hitherto for impregnation, there is not a single one which, while hastening absorption, is absolutely non-irritant, and as a medium of this kind is a necessity for patients with a sensitive skin and especially for children, Göppert has for about 8 years tried a mixture of equal parts of alcohol (96 p. c.) and glycerin, which has proved most successful in the Children's Clinic in Göttingen. He worked upon the hypothesis that, on the one hand, alcohol in the form of alcohol compresses prevents irritation, while on the other hand, glycerin is capable of checking the corrosive and necrosis-producing action of phenol. It therefore seemed worth while to try whether glycerin might not counteract the excessively irritant properties of alcohol. This, according to Dörken, is the case. He therefore employs it whenever compresses moistened with alcohol, aluminium acetate or other impregnating substances are indicated, as for example in suppurative adenitis, mastitis, cellulitis, inflammation of the navel in the newborn and similar cases. It is employed in the same way as are moist compresses. Broncho-pneumonia forms a further indication for the use of the alcohol-glycerin mixture, as, in this condition, rubbing with brandy and similar drugs prescribed as powerful cutaneous irritants is apt to give rise to sores, and this is prevented by the glycerin.

\*) Compare Merck's Report 1911, p. 159.

Gosio, Gazzetta degli ospedali e delle cliniche 1911, Vol. 109,

Münchener medizinische Wochenschrift 1912, No. 7, p. 394.

Dörken, Therapeutische Monatshefte 1912, No. 10, p. 711.

The alcohol-glycerin mixture is also useful for compresses for the throat in sensitive children. It has proved efficacious and non-irritant in colds. Clinical experiences tally with the pharmacological investigations carried out by Dörken. According to him, glycerin-alcohol mixture is a preparation which gives rise to the minimum degree of cutaneous irritation, while possessing strongly antiphlogistic properties, and is destined to take the place of the customary moist compresses, especially among children (newborn and sucklings).

Sustmann discusses the use of glycerin compresses for the treatment of wounds in veterinary practice. For open wounds glycerin ointment may be used in place of glycerin and may be combined, if desired, with boric acid, tannin, iodoform, etc. It has proved of service in cases of pressure sores caused by the saddle or harness, eczema, cutaneous wounds, ulcers and injuries of the knees. With the use of glycerin compresses, the action of glycerin is still more effective. Even chronic ulcerative wounds are very favourably influenced by the glycerin, and inflammatory conditions of the connective tissue, which frequently accompany wounds of this nature, entirely disappear. Glycerin compresses are, however, of little use by themselves in spontaneous cellulitis or cellulitic processes.

#### Grotan.

The strongly antiseptic action of chloro-meta-cresol\*) induced M. Schottelius to investigate the utility of various chloro-cresol preparations for purposes of disinfection. As a result of his investigations, he decided in favour of a chloro-cresol-alkali compound, which is placed on the market in the form of tablets, under the name of "Grotan". A 0.5 p. c. solution of this preparation, according to the author's investigations, destroys all infective germs within 5 minutes, and a 0.25 p. c. solution within 20 to 30 minutes. Anthrax spores, alone, which, according to the author, need scarcely be considered in practice as infective agents for human beings, are more resistant and are only destroyed by a 1 p. c. solution after 20 minutes' continuous action. According to this, grotan is

Sustmann, Deutsche tierärztliche Wochenschrift 1912, No. 12. —  
Berliner tierärztliche Wochenschrift 1912, No. 40, p. 740.

\*) Compare Merck's Reports 1910 and 1911.

Schottelius, Münchener medizinische Wochenschrift 1912, No. 49,  
p. 2674.

a substance with a powerful bactericidal action. The author also established that grotan is only slightly toxic and gives rise to practically no cutaneous irritation. It is almost odourless, and only dissolves in water to the extent of 2 p. c., so that the inadvertent use of more highly concentrated solutions cannot occur. On the other hand, 1 to 2 p. c. solutions should suffice to comply with even high demands, as a 0·5 p. c. solution is sufficient for ordinary purposes.

### Guaiacol.

Guaiacol and tincture of guaiacum, as is well known, were suggested some time ago as tests for distinguishing boiled from unboiled milk\*). K. Schern and W. Schellhase have recently found that the simultaneous employment of these two substances leads to more satisfactory and more definite results. If old guaiacum resin tincture is poured on to the surface of milk, as is well known, a blue ring forms if the milk has not been boiled, but remains absent with boiled milk. If it is desired to use the fresh tincture, a few drops of hydrogen peroxide solution should be used with it, as fresh tinctures contain no peroxide. If instead of tincture of guaiacum, guaiacol and hydrogen peroxide solution are employed, a salmon coloured to red ring is produced by unboiled milk, and no coloration by boiled milk. But, according to the authors mentioned above, tinctures of guaiacum may be useless for the reaction, as they do not give a blue colour with unboiled milk. Tinctures of this kind are rendered very sensitive by the addition of an equal volume of guaiacol. The authors therefore suggest that instead of tincture of guaiacum, a mixture of tincture of guaiacum and guaiacol be used, as it is even more sensitive than is an effective tincture of guaiacum. A peroxide is added to the reagent. The formula suggested by the two authors is as follows:

Rp. Resin. guaiaci	10·0 grammes
Guaiacol.	10·0 grammes
Perhydrol (3 p. c.) gutt.	I
Alcohol. absolut.	80·0 grammes

\*) Compare the Reactions of Arnold-Weber, Arnold-Mentzel, Carcano, Dupouy and Bruère in Merck's Reagenzien-Verzeichnis. Schern-Schellhase, Berliner tierärztliche Wochenschrift 1911, No. 48, p. 868 and 1912, No. 13, p. 221.

If a few drops of this reagent are layered on to the surface of unboiled milk, a very dark blue ring is immediately produced. Usually a pale reddish ring may be seen beneath it, caused by the guaiacol reaction which takes place simultaneously.

### Hectine.

Hectine (sodium benzol-sulphon-p-amido-phenyl-aronate)\*) has been reported upon by W. Sterling, S. O. Jermulowicz, F. Balzer, Micheleau, Gaucher and Guggenheim.

Sterling and Jermulowicz treated several cases of secondary, tertiary and hereditary syphilis with single doses of 0.2 grammes (3 grains) of hectine and came to the following conclusions: Intramuscular injection of the preparation causes little pain and has no injurious effect upon the internal organs. The general therapeutic effect of the drug is to improve the general health and the body-weight and to cause an increase in the erythrocytes, particularly in its action upon syphilitic lesions. It causes the disappearance of secondary and tertiary symptoms without the help of other drugs, but not more quickly than by treatment with mercury. But it does not kill the spirochetes, does not protect against recurrences and has no influence upon the Wassermann reaction. Its effect on lymphatic gland swellings also appears to be slight. Balzer suggests the use of 2 to 3 grammes (30—45 grains) for a complete course of hectine treatment; single doses of 0.1 to 0.2 grammes ( $1\frac{1}{2}$ —3 grains) are injected at intervals of two days. In order to avoid injury, the ears and eyes should be examined before commencing the injections, and the absence of affections of the acoustic apparatus, the retina and the optic nerve established. The hectine ampoules should not be kept in the light, as the solution of hectine is readily and rapidly decomposed in the light. The favourable opinion of these authors was confirmed by Micheleau, who obtained an apparently complete cure by several series of injections in a case showing syphilitic symptoms of the tongue.

\*) Compare Merck's Report 1911.

Sterling-Jermulowicz, Medicyna 1912, p. 275.

Balzer, Presse médicale 1911, No. 102, p. 1059.

Micheleau, Presse médicale 1912, No. 25, p. 252.

Gaucher-Guggenheim, Presse médicale 1912, No. 12, p. 121.

Gaucher and Guggenheim have carefully investigated the possibility of hecine treatment causing injury to hearing. As this possibility cannot be denied if disturbances of hearing are present, the authors are in favour of small doses of 0·1 grammie ( $1\frac{1}{2}$  grains) of hecine, if disturbances occur, of the employment of some other drug.

### Hediosit.

Glycoheptoic acid lactone, which I mentioned in my last Annual Report, is now on the market under the name of "Hediosit".

Previous investigations on the excretion of glycoheptoic acid lactone, according to Kohshi Ohta, require correction, because the acid excreted in the urine was estimated directly by the polariscope. The author, however, found that no unaltered glycoheptoic acid lactone is present in the urine, but that the sodium salt of glycoheptoic acid is present, which has an optical rotation opposite to that of lactone. In order to obtain the correct figures for excreted glycoheptoic acid, the urine must be boiled with hydrochloric acid and allowed to stand for 24 hours. If the urine is then polarised, the correct values will be obtained. The author's investigations did not determine whether products of decomposition of lactone are formed in the organism. With regard to the absorption of the drug, it has been found that it is partially destroyed, but that some of the unaltered substance is excreted in the faeces and that, on the whole, the excretion of glycoheptoic acid is greater than was formerly supposed. The author was, however, able to confirm the innocuousness of glycoheptoic acid lactone.

E. Lampé and J. Kretschmer report upon the use of hediosit in the treatment of diabetes mellitus. Lampé gave 30 grammes (1 oz) of hediosit a day, divided into 3 portions, for the most part in severe cases, and in the majority of cases observed a decline in the excretion of sugar. It had no effect upon the excretion of acetone, from which the author concludes that hediosit does not form glycogen. Lampé is also not able to offer a better explanation regarding the action of the drug than are other authors. But he considers it certain

Kohshi Ohta, Biochemische Zeitschrift 1912, Vol. 38, p. 421.

Lampé, Therapie der Gegenwart 1912, No. 6, p. 244.

Kretschmer, Berliner klinische Wochenschrift 1912, No. 47, p. 2221.

that hediosit is a sweet substance, innocuous to the diabetic, which usually effects a diminution in the glycosuria, and is well tolerated in the amounts mentioned, besides having a favourable effect on the general health. For persons in whom the medication readily induces diarrhoea and loss of appetite, Lampé recommends a single dose of 10 grammes ( $\frac{1}{3}$  oz) a day, or 10 grammes ( $\frac{1}{3}$  oz) may be given 3 times a day every 3 to 4 days.

Kretschmer illustrates the increase of tolerance for carbohydrates in a case of diabetes. On those days on which hediosit and 100 grammes of bread were given, the glycosuria fell to 2·1, and on the following day, probably in consequence of the after-effects of the medication, to 1; while after the administration of 75 grammes of bread without hediosit it rose to 5·3.

Kraner, after having given hediosit to 19 patients, most of whom were severely ill, came to the following conclusions: Sugar excretion falls on an average by 5·3 grammes during the employment of hediosit and rises considerably on leaving off the drug. The urine passed during the night contains less sugar than that passed during the day. Different patients show different degrees of sugar excretion, but the decrease mentioned above usually occurs, with transient rises at times. The action of hediosit usually begins within 12 to 24 hours. The author also observed an influence on the increase in amount of the urine. Hediosit increases the action of the more intensive limitation of diet and increases the effect of the vegetable and egg days. In the majority of cases hediosit also appears to effect a diminution in the excretion of acetone. It has no evident influence on the alteration of body-weight. In 26 p. c. of the cases treated, hediosit led to diarrhoea, and in 15·8 p. c. to loss of appetite and vomiting, a daily dose of 30 grammes (1 oz) being given. Hediosit is inferior to saccharin in sweetening power. It will probably for the present be chiefly used in clinical treatment.

### Hegonon.

This silver albuminate preparation, which had been tested by Klingmüller, was investigated by R. Garin with re-

Kraner, Deutsche medizinische Wochenschrift 1912, No. 51, p. 2416.  
Klingmüller, Merck's Report 1910, p. 207.

Garin, Klinisch-therapeutische Wochenschrift 1912, No. 4, p. 111.

gard to its therapeutic value in gonorrhœal processes. The results of his investigations, though not so favourable as those of the first named author, yet show that hegonon represents a useful remedy for gonorrhœa, equal in value to other silver albuminate preparations. The author's results are as follows:

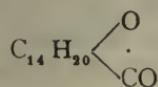
"Five abortive cases, free from gonococci after 1 to 3 days and shown by longer observation to be definitely cured. These were all cases of superficial gonorrhœa, which accounts for the rapid and permanent therapeutic effect. 10 cases of anterior deep gonorrhœa. Free from gonococci after 8 to 38 days; control investigations were, of course, carried out in order definitely to determine the effect. 5 cases were not free from gonococci for 50 days and more, and we were obliged to resort to other methods of treatment. In one case the treatment by injections gave rise to a complication (peri-urethral abscess). Of the 16 cases of posterior gonorrhœa (prostatitis, spermatocystitis), which we treated by means of irrigations of hegonon according to Janet, combined in some cases with massage of the prostate or of the vesicula seminalis, the gonococci disappeared after 5 to 26 days in 4 cases, but in the other cases we were able to demonstrate gonococci even after 50 days. We did not observe epididymitis as a complication."

The author used a 0·25 p. c. solution of hegonon for injections, and a 0·025 to 0·1 p. c. solution for urethral irrigation, the solutions always being freshly prepared before use.

### Helenin.

A recent publication by A. Hecht on the therapeutic value of helenin as a remedy in phthisis leads me to give a short account of this preparation here as, in the author's opinion, it deserves further consideration in the treatment of pulmonary tuberculosis.

Helenin (alantolactone, alantcamphor) is found in the root of *Inula Helenum*. It is the lactone of alantic acid and corresponds to the formula



Hecht, Münchener medizinische Wochenschrift 1912, No. 42, p. 2277.

— Compare also Münchener medizinische Wochenschrift 1905, No. 9, p. 416 and Therapeutische Monatshefte 1904, p. 437.

Helenin is insoluble in water, but dissolves readily in ether, alcohol, petroleum ether, chloroform, benzol and fatty oils. It melts at about 74° C.

The root of Inula also contains iso-alantolactone, a body isomeric with helenin and very similar to helenin in external characters and in solubility. Iso-alantolactone melts at 115° C.

According to Bokenham, helenin has an inhibitory effect on the growth of tubercle bacilli in a dilution of 1 in 10 000. His pharmacological experiments also show helenin to be of value in tuberculosis. However, the preparation was used with success in tuberculosis, whooping-cough and bronchial affections even before the publication of Bokenham's communications. Valenzuela recommended it in the year 1884, in single doses of 0.01 gramm (1/6 grain) and in daily doses of 0.1 gramm (1 1/2 grains), for bronchial affections. The value of helenin was described more in detail by Hanika, who used it with good results, both internally and subcutaneously, in tuberculosis. It is also said to be of value in cholera\*). Harmonic and Parisot prescribed it with excellent results in leucorrhœa accompanied by catarrhal endometritis, while according to these observers it proved ineffectual in gonorrhœal urethritis.

The very beneficial results obtained by Hecht since 1897 by the use of helenin in pulmonary tuberculosis favour the wider employment of the drug in therapeutics. This can readily be effected, since helenin is completely devoid of injurious and unpleasant after-effects. It must be understood from the start that it is not a specific against tuberculosis, but, according to Hecht, it is quite as effective as are the modern creosote preparations. The author even succeeded in bringing about a considerable improvement in the general health and in the condition of the lungs in cases which had not been benefited by creosotal, etc., so that the patients enjoyed good health for

Bokenham, Therapeutische Monatshefte 1892, p. 145. — British Medical Journal 1891, II, p. 838.

Valenzuela, Merck's Bericht 1890, p. 34. — Compare also Marpmann, Breslauer ärztliche Zeitschrift 1887, No. 5, Medizinisch-chirurgische Rundschau 1887, No. 8, Pharmazeutische Zeitung 1887, No. 36, p. 252.

Hanika, Heilung der Lungenschwindsucht, München 1897 (Published by Seitz and Schauer).

\*) Compare Merck's Report 1890, p. 34.

Harmonic-Parisot, Répertoire de pharmacie 1891, p. 481.

many years. 0·01 to 0·3 grammes ( $\frac{1}{6}$ —5 grains) may be given as a single dose and 1 grammme (15 grains) as a daily dose. The following prescription has answered particularly well:

Rp. Quinin. cinnamyl. [or Potassium Guaiacol-Sulphonate Helenin (Merck) Sod. arsenic.	5·0	grammes (75 grains)
	10·0	„ (150 grains)]
	2·5	„ (40 grains)
	0·1—0·15 gramme	(1 $\frac{1}{2}$ —2 $\frac{1}{3}$ grains)
Extract. Nuc. vom.	1·0—1·5	grammes (15—24 grains)
	M. Et. pil. No. 100	

Sig : 2 pills to be taken 3 times a day after meals

L. Rénon prescribes helenin in combination with peronin and thebaine to combat the cough in phthisis, in the form of powders or pills containing

Peronin	0·01	gramme	( $\frac{1}{6}$ grain)
Thebaine	0·01	"	( $\frac{1}{6}$ "
Helenin	0·02	"	( $\frac{1}{9}$ "

for a dose. Two doses are given daily at intervals of about 5 hours.

### Hepin.

A few years ago Römer and Much suggested a method by means of which the hydrogen peroxide added to milk as a preservative could be decomposed. It was intended to remove the disagreeable taste which hydrogen peroxide imparts to milk. For this purpose they used a catalytic agent prepared from liver by a special process, which is capable of completely converting hydrogen peroxide into oxygen and water. On account of the increasing interest which has been shown in recent years for oxygen baths, it was desirable to prepare the catalytic agent from liver in the cheapest way possible, so that by the help of hydrogen peroxide, which can be obtained readily and cheaply in suitable quality and quantity, oxygen baths might be prepared without employing chemicals liable to stain. For this purpose a sterilized extract of liver is issued in ampoules of 5 c.c. under the name of "hepin".

0.075 grammes of hepin liberates 1 litre of oxygen from 100 c.c. of a 3 p.c. solution of hydrogen peroxide, so that by its use oxygen baths can be prepared in the simplest possible manner. According to R.v.Hoesslin and Sardemann, 1 litre of solution of hydrogen peroxide (3 p.c.) and the contents of one ampoule of hepin are added to a full sized bath at 33—35° C. The hydrogen peroxide solution is first mixed with the total amount of bath water and then the hepin mixed with 1 litre of water is added. Oxygen is at once liberated and in 10 to 15 minutes the bath water is full of little bubbles. Now the bath is ready for use. The liberation of oxygen continues for some time, so that the body is covered with innumerable little bubbles of gas. Thus these oxygen baths, like carbonic acid baths, cause moderate stimulation and hyperæmia of the skin, with the corresponding results.

It is evident that these oxygen baths, with their slow liberation of oxygen, are much superior to baths supplied with oxygen gas under pressure. As it is important to employ a solution of hydrogen peroxide with a reliable content of  $H_2O_2$ , I issue a suitable solution under the name of "Hydrogen peroxide Merck, rendered stable, for baths, 3 or 6 per cent".

The decomposition of hydrogen peroxide used to preserve milk is of importance in the analysis of milk, when testing for nitrates. Utz therefore suggests that the milk should be heated to 35° C. and hepin added, in order to remove the hydrogen peroxide which would otherwise interfere with the diphenylamine reaction carried out subsequently.

### Heroin.

Morphine is well known to be a valued drug in cardiac asthma. It acts not only by very rapidly diminishing the subjective dyspnoea, but also by decreasing the objective number and depth of the respirations, so that the patients drop into a refreshing sleep. As the attacks of asthma usually

Hoesslin, Münchener medizinische Wochenschrift 1911, No. 47, p. 2506.

Sardemann, Münchener medizinische Wochenschrift 1911, No. 17, p. 925.

Utz, Pharmazeutische Zentralhalle 1912, p. 1158.

occur at night, it is advisable, according to A. Fraenkel, to give the injections of morphine in the evening. They may be given with good results for many days, in case their repetition is required, until the congestion in the pulmonary circulation has been completely removed, as a result of the intercurrent administration of digitalis. But if digitalis treatment fails and morphine injections have to be continued for a prolonged period, the patients gradually become habituated to the morphine and the strength and number of the injections have to be increased, which may, in various ways, cause injury to the patients. Fraenkel therefore prefers heroin (hydrochloride) which is known to depress the excitability of the respiratory centre, so that the number of respirations is diminished, while their depth is increased. In giving heroin by subcutaneous injection, the author observed that doses of 0.01 to 0.015 grammes ( $\frac{1}{6}$ — $\frac{1}{4}$  grain) are more effective than morphine and that the effect is scarcely lessened even when the drug is administered for many weeks. Only rarely do patients prove refractory to heroin, as they may do to morphine, so that another drug has to be resorted to. The author has not observed either morphine or heroin to have an injurious effect upon the cardiac action. Accidents may be avoided if 0.005 grammes ( $\frac{1}{12}$  grain) heroin is injected at first, and the dose gradually increased to 0.01 grammes ( $\frac{1}{6}$  grain) when the small doses no longer have the desired effect. Fraenkel is strongly opposed to exceeding 0.015 grammes ( $\frac{1}{4}$  grain). The author does not, however, consider heroin to be a dangerous drug, as others have assumed. The use of a combination of morphine and heroin has proved valuable in many cases. It should be prescribed thus: morph. hydrochl. 0.2 grammes (3 grains), heroin hydrochl. 0.1 grammes ( $1\frac{1}{2}$  grains), aq. destill. 10.0 grammes (170 min.); of this 4 divisions to half a syringeful should be injected = 0.008 grammes ( $\frac{1}{8}$  grain) of morphine hydrochloride and 0.004 grammes ( $\frac{1}{16}$  grain) of heroin hydrochloride and the dose increased, if necessary, up to 0.01 grammes ( $\frac{1}{6}$  grain) of morphine and 0.005 grammes ( $\frac{1}{12}$  grain) of heroin.

H. Langer reports upon his pharmacological experiments, which he carried out in order to investigate the excretion of, and the habituation to, heroin. According to these, heroin is

excreted by rabbits and dogs chiefly in the urine, to a less degree in the faeces. In rabbits definite habituation to the drug could not be demonstrated, while dogs were found to become habituated to the narcotic action, but not to the spasmodyic action. This shows that habituation to non-lethal doses is alone possible, and it is purely functional in Hausmann's sense. The death of the animals is caused by the spasmodyic action of heroin and not by the central paralysis of the respiratory centre; the author proves this by showing that, on suppression of the spasmodyic action by ether anaesthesia, larger doses can be administered.

**Hexamethylenetetramine.** (Amphotropin, Blenaphrosin, Cystopurin, Hexal, Urotropine.)

The literature of the past year includes several interesting reports upon this well-tested vesical antiseptic.

E. Zak succeeded in showing that urotropine, when administered internally, not only passes into the saliva, as was shown by Hanzlick, but is found in the sputum and is excreted in the bronchi. This discovery favours the employment of hexamethylenetetramine as a pulmonary disinfectant. In the author's opinion, it is specially indicated in ulcerative processes of the lung, in pulmonary tuberculosis, gangrene and bronchiectasis; but his own experiments are too insignificant to afford proof of this. Theoretically, the author's view must probably be accepted, as hexamethylenetetramine is well known to be an efficacious antiseptic, even without being decomposed. On the other hand, if formaldehyde is split off, its action is wholly or partially neutralized by being anchored to albuminous substances. Experiments with the preparation may therefore prove promising. Hexamethylenetetramine also appears to pass into the eye, but Zak is undecided whether this always happens and whether this fact is of therapeutic value. Finally, the author draws attention to the (well known) action possessed by hexamethylenetetramine of checking fermentation, which might prove of value for the disinfection of the stomach in pyloric stenosis. The action is due to the formaldehyde split off by the acid gastric juice. In the

Zak, Wiener klinische Wochenschrift 1912, No. 4, p. 151.

Hanzlick, Journal of the American Medical Association 1910, Vol. 54, p. 1940.

cases observed by Zak, the drug was well tolerated; he gave daily doses of 2 to 4 grammes (30—60 grains). He further observed that in a case of ulceration at the pyloric end of the stomach, the administration of 0·5 gramme ( $7\frac{1}{2}$  grains) twice a day caused the gastric juice to lose its unpleasant odour, the offensive odour of the eructations disappearing at the same time. The employment of urotropine as an intestinal antiseptic, according to Zak, offers little promise of success.

Urotropine, on the other hand, is probably beneficial in various skin diseases. After the internal administration of the drug (4 to 6 grammes [60—90 grains] a day) to patients with herpes zoster or erythema exsudativum multiforme and bullous, O. Sachs was able to demonstrate the presence of formaldehyde in the vesicles, and in impetigo contagiosa in the crusts. Hence a beneficial influence may be expected from the use of urotropine in these diseases.

Zak's assumption that hexamethylenetetramine would prove of value in affections of the respiratory passages is confirmed in the communications of A. Eisenberg, M. J. Breitmann and Douglas Vanderhoof. Vanderhoof gave as a routine 0·6 gramme (10 grains) dissolved in a full glass of water four times daily for three to seven days, and obtained very satisfactory results in "colds", and in acute and chronic bronchitis. It not only shortens the duration of the "cold" and guards against complications, but also prevents the extension of the morbid process to the secondary sinuses of the nose. In acute bronchitis it is said that the preparation is superior to all the drugs usually employed, but that in chronic bronchitis it is only successful if the process has not already led to deep-seated changes. According to Eisenberg, hexamethylenetetramine must be given in large doses if it is required to act promptly. In such cases secondary effects of the preparation must be expected and it must be remembered that the German pharmacopœia gives 1 gramme (15 grains) as the maximum single dose and 3 grammes (45 grains) as

Sachs, Wiener klinische Wochenschrift 1912, No. 4, p. 153.

Eisenberg, Journal of the American Medical Association 1912, 29<sup>th</sup> June.

Breitmann, Praktitscheski Wratsch 1911, No. 47.

Vanderhoof, Journal of the American Medical Association 1912, No. 5.

the maximum daily dose. W. D. Fullerton, under certain conditions, is in favour of large doses. He believes that as an antiseptic for the protection of the cerebro-spinal fluid doses up to 10 grammes (150 grains) may be given. In one case of surgical treatment for suppuration of the frontal sinus in a woman, he gave 2·4 grammes (40 grains) of hexamethylenetetramine a day for 2 days before the operation and 12 grammes (200 grains) more in the 4 days following the operation. Helmitol (hexamethylenetetramine methylene-citrate) was now administered in doses of 1 gramme (15 grains) three times a day; unfortunately, however, through a mistake, the patient received 3 grammes (45 grains) more of the drug during the day. As a consequence, hæmaturia occurred, small blood clots as well as pieces of bladder membrane were passed. The author states that the symptoms observed are conclusive evidence that the trouble was purely a medicinal cystitis. Hæmaturia of a mild grade has been encountered after the use of the drug, but clears up rapidly on its discontinuance.

Breitmann prescribed urotropine in follicular tonsillitis and found that the course of the malady was milder than when the customary treatment was adopted alone. In alimentary toxæmia he also obtained good results with the drug, especially in combination with aspirin.

S. J. Crowe employed hexamethylenetetramine in various infective diseases of the urinary, respiratory and biliary passages, and of the nervous system, and obtained good results, especially in affections of the gall-bladder occurring in the course of typhoid fever. In operations on the cranium urotropine proved useful as a measure for guarding against meningitis.

van Caneghem also discusses the value of urotropine in meningitis. He states that a daily dose of 0·1 gramme ( $1\frac{1}{2}$  grains) of the drug for each kilogramme of body-weight checks the growth of bacteria in the cerebro-spinal fluid of the normal individual. His pharmacological experiments on animals show that urotropine acts chiefly as a prophylactic;

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Fullerton, Journal of the American Medical Association 1912,  
January 13.

Crowe, Bulletin of the Johns Hopkins Hospital 1912, Vol. 23, p. 255.  
Caneghem, Deutsche medizinische Wochenschrift 1912, No. 22,  
p. 1068. — Zentralblatt für die gesamte Therapie 1912, No. 9,  
p. 480.

if the morbid process is too far advanced, not much is to be expected from its use. When the liquor has once become active by the immigration of leucocytes, urotropine does not increase its activity towards staphylococci, or at most only to a slight extent.

G. Malan tried urotropine, according to Chauffard's suggestion, in typhoid and, for comparison, treated some of his patients without this drug. The cases treated with urotropine showed a strikingly better result than the others; but the author does not at present attribute this to the urotropine, as the nature of the disease does not permit a definite opinion to be formed. Thus he reports that in one month all the cases, whether treated with or without urotropine, ran a favourable course.

According to Humphrey Prouty, a further indication for hexamethylenetetramine is secondary orchitis, following tonsillitis. After acetyl-salicylic acid had been administered without effecting an improvement, the author gave 0.75 gramme (12 grains) of hexamethylenetetramine every 6 hours, and this medication brought about an improvement and a cure in a comparatively short time.

L. Rénon and Ch. Richet carried out therapeutical experiments with urotropine to ascertain its disinfecting power on bile and found its action in phlebitis to be unreliable. In the majority of cases, however, it rapidly brings about improvement. A dose of 0.5 gramme ( $7\frac{1}{2}$  grains) was given twice a day.

Experiments with hexamethylenetetramine also appear to promise a certain amount of success in poliomyelitis of children, though no definite conclusion can as yet be drawn from the communications of A. Gullström and A. Josefson. Josefson suggests the following method of employment, which he tried in the hospital for infectious diseases in Stockholm. Hexamethylenetetramine is given as a prophylactic and a curative agent in a large amount of water. A teaspoonful or a tablespoonful of a solution of hexamethylenetetramine (10:300) is given every 2 hours during the day, and every

Malan, Gazzetta degli ospedali e delle cliniche 1912, No. 31.  
Prouty, Journal of the American Medical Association 1912, April 20.  
Rénon-Richet, Presse médicale 1912, No. 87, p. 879.  
Gullström, Allmäna Svenska Läkartidning 1911, p. 759.  
Josefson, Allmäna Svenska Läkartidning 1911, p. 778.

3 hours during the night, in milk, water, fruit syrup and similar beverages. A daily dose for children aged 1 to 5 years is 1·5 to 4 grammes (24—60 grains), aged 5 to 15 years 4 to 6 grammes (60—90 grains), and for older patients 6 to 10 grammes (90—150 grains), or even more if required. When the fever has subsided the dose should be reduced, but the medication should be continued for about a week longer. The nursing staff should also be prophylactically treated with hexamethylenetetramine. It is said that no harm is attached to the high dosage, but the author has in several cases observed irritation of the bladder with severe strangury and vesical haemorrhage, which disappeared on the discontinuance of the drug. But the value of hexamethylenetetramine in infantile paralysis has not yet been established, and further tests of the method of treatment described by the author are required.

In place of hexamethylenetetramine for certain indications, its salts and combinations with other substances are used in therapy, e. g., the salicylate, camphorate, sulpho-salicylate, etc., of hexamethylenetetramine. Special interest has recently been shown for the sulphonate of hexamethylenetetramine, known under the name of "hexal".

Hexal is hexamethylenetetramine sulpho-salicylate,  
 $(CH_2)_6 N_4 \cdot SO_3 H \cdot C_6 H_3 (OH) COOH$ .

It forms white crystals, readily soluble in water, slightly soluble in alcohol, and having a pleasant, acid taste. The composition of the preparation corresponds to about 39·1 p. c. of hexamethylenetetramine and 60·9 p. c. of sulpho-salicylic acid.

According to S. Boss, hexal is an excellent vesical anti-septic, which may be safely taken for weeks. It does not give rise to gastric disturbances, nor to irritation of the urinary apparatus. Its action is most evident in acute vesical catarrh, whether caused by extension from neighbouring parts, as in gonorrhœal cystitis, or by chill, urethral stricture, hypertrophy of the prostate or paresis of the bladder of central origin, tabes, myelitis, etc. Above all, the drug removes strangury and scalding in the urethra, symptoms which are alleviated in 2 to 3 days by hexal medication and disappear on an average in 4 to 5 days. It also rapidly clears up turbid and bloody urine, the alkaline urine becoming acid in about a week, while the haemorrhage is checked.

The action of hexal is equally favourable in chronic vesical trouble, especially in cystitis due to prostatic disease and in calculus cystitis, if the medication is combined with suitable local treatment.

Boss summarises the advantages of hexal as follows: "1. Powerful sedative action due to sulpho-salicylic acid. 2. Energetic bactericidal action, due to formaldehyde plus sulpho-salicylic acid. Both antiseptics impart to the urine such a high antiseptic power that it is enabled to check the development of all bacteria. 3. Distinct astringent action, due to the introduction of the sulphonic acid group into the salicylic acid molecule. The sulpho-salicylic acid precipitates albumin and effects the contraction of vessels of the hyperæmic vesical mucous membrane."

Indications for the employment of hexal are: acute and chronic inflammation of the bladder, gonorrhœal inflammation of the posterior urethra, and bacterial diseases, such as pyelitis and pyelonephritis, and also uric acid deposition in the kidney and bladder.

As a rule 3 to 4 or 6 daily doses of 1 gramm (15 grains) of hexal, given in aqueous solution after meals, are sufficient. When the severe inflammatory symptoms have subsided, the amount may be reduced to 2 or 3 doses.

The author's results were confirmed by E. Frank and K. Seegers. Frank found that renal irritation, when present at the same time, was favourably influenced by hexal, and that besides the bactericidal action of the drug, a marked diminution of the leucocytosis occurred. If the drug were discontinued, the bacterial content very quickly returned to the original amount, the leucocytosis recurring at the same time, in all those cases in which the source of infection did not lie entirely in the renal pelvis, the bladder and urethra; particularly, therefore, in cases accompanied by affections of the female adnexa or of the male genital glands or of the digestive tract.

Seegers prescribed hexal with good results for chronic catarrh of the bladder, and for this condition combined with chronic nephritis, and also for paralytics suffering from paralysis of the bladder and from chronic irritative conditions.

The camphor salt of hexamethylenetetramine is put on the market under the name of "amphotropin". It is a white, crystalline powder, soluble 1 in 10 of water. According to G. Fischer, it is useful in vesical and renal disease, in milder forms of uric acid diathesis and as a prophylactic in infective diseases. It should not be given in acute cystitis unless combined with alkaloids. The dose is 0·5 to 1 gramm (7½—15 grains), three times a day\*).

Cystopurin\*\*) (Hexamethylenetetramine sodium acetate) was successfully prescribed by Walz in gonorrhœa, to guard against cystitis, or for existing cystitis. The author was satisfied with the action of 3 to 6 grammes (45—90 grains) of the drug daily. He specially points out that it checks the growth of gonococci and increases the resisting power of the mucous membranes, without giving rise to gastric or intestinal trouble.

Blenaphrosin, a combination of hexamethylenetetramine and potassium nitrate and kawa-kawa is recommended by M. Herbst for the treatment of gonorrhœa, cystitis, hypertrophy of the prostate, sexual hyperæsthesia in neurasthenic subjects, and vesical irritability. The preparation is issued in the form of capsules and suppositories. The author prescribed 2 to 4 capsules internally 3 times a day, or 1 suppository rectally twice a day.

### Histopin.

Histopin\*\*\*) was tried by S. C. Beck in a number of cases of furunculosis and folliculitis, impetigo, sycosis coccogenes, eczema intertrigo, and acne vulgaris. For prophylactic purposes he used histopin-gelatin, lightly applied by means of cotton wool, and for curative purposes histopin ointment, applied superficially in the form of an ointment dressing, and to deeper furuncles, which have burst or have been drained by means of Bier's suction apparatus, in the form of tampons. His results are as follows:

Fischer, Folia urologica 1912, No. 3.

\*) Compare Zentralblatt der gesamten Arzneimittelkunde 1912, No. 5, p. 248.

\*\*) Compare Merck's Reports 1907 and 1909.

Walz, Therapie der Gegenwart 1912, No. 6, p. 287.

Herbst, Allgemeine medizinische Zentralzeitung 1912, No. 36, p. 469.

\*\*\*) Compare Merck's Report 1911.

Beck, Medizinische Klinik 1912, No. 22, p. 907.

Superficial staphylococcic infections of the skin and folliculitis, small boils and pustules of babies were, as a rule, rapidly cured, often in the course of 3 to 4 days, the pustules drying up and the inflammatory area disappearing. Occasionally an eruption of numerous fresh pustules immediately follows the first application of histopin, but these soon disappear and do not hinder further treatment. Deeper infiltrations are less influenced by histopin treatment, but tend to heal well under the action of the drug after operation has been performed. In impetigo, on the other hand, the action of histopin is unreliable; the author attributes this to the disease germs, for streptococci are present here as well as staphylococci. In the cases which respond to treatment, the cutaneous surface to which the drug has been applied probably remains immune against staphylococcic infection for a considerable time. In one case the author observed a recurrence, i. e., fresh infection, after 4 months.

In Beck's experience, the action of histopin sets in rapidly. If, therefore, no definite improvement has taken place by the end of the first week of treatment, other methods should be adopted, as histopin will probably be ineffectual in these cases.

Von Boltenstern also observed the rapid healing of a furuncle in the axilla by the use of histopin after incision. The inflammatory symptoms soon disappeared, the hyperæmic area became pallid and the surrounding hard infiltration subsided.

Blepharitis, according to von Marenholtz, forms another indication for histopin. After removing the scabs, etc., and opening any pustules, histopin ointment is well rubbed into the edges of the eyelids between the eye-lashes. After an apparent cure, histopin-gelatin should be applied prophylactically for some time longer—about 8 to 10 days. The author considers that the chief advantage of histopin treatment is that it shortens the period of treatment. In cases of chronic blepharitis, which had undergone treatment for many months, he brought about a complete cure in 10 to 14 days by the use of histopin. He also obtained

Boltenstern, Deutsche Ärztezeitung 1912, No. 18, p. 281.

Marenholtz, Wochenschrift für Therapie und Hygiene des Auges 1912, Vol. 16, No. 1, p. 2.

good results in styes and pustules after incision and the application of histopin. In two elderly diabetic patients, who had for many years been troubled with eczematous rashes of the face with the formation of furuncles and recurring blepharitis, both the skin disease and the disease of the eyelids improved markedly, while the tendency to recurrence was greatly diminished.

### Hydrastinine Hydrochloride.

Hydrastinine has up to now been prepared by oxidation of hydrastine, an alkaloid obtained from the root of *Hydrastis canadensis*, and on account of the high price of this drug, it was a very expensive preparation. Recently various methods have been discovered of preparing the substance synthetically.

Martin Freund (Frankfort o/M.) took out a patent for a process of preparing hydrastinine and analogous bases from berberine (German Patent No. 241,136, transferred to E. Merck, Darmstadt). Hermann Decker (Hanover) obtained a patent for a process for preparing hydrastinine salts, in which he starts from safrol or from heliotropin (German Patent No. 234,850). This process is adopted by the Farbenfabriken vorm. Friedr. Bayer & Co., Elberfeld.

The price of hydrastinine has consequently fallen considerably, which permits of its more extensive use. Therefore a brief reference will be made in the following to the more important therapeutic data in the literature of hydrastinine.

Pharmacological and physiological investigations have been carried out by W. Kramm and J. de Vos. According to these, hydrastinine possesses a cumulative action in cold-blooded animals, but not in warm-blooded animals. Hydrastinine is considerably less toxic than hydrastine, and does not, like the latter, exhibit a tetanising, but a paralysing action. In experiments on warm-blooded animals (the author used dogs) habituation to hydrastinine can be effected by gradually increasing doses. The dose may thus be increased from 0.1 gramme to 2.6 grammes without causing poisoning, and the continuous administration does not give rise to gastric or intestinal trouble. The author was unable to discover an abortive

Kramm, Dissertation Berlin 1894.

de Vos, Archives de pharmacodynamie 1895, Vol. 2, No. 1.

action either for hydrastinine or for hydrastine. E. Falk showed by pharmacological experiments that hydrastinine increases the contractility of cardiac muscle, but that it is not a cardiac poison either in cold-blooded or in warm-blooded animals. It causes lasting, powerful vascular contraction by direct action on the vessels, and also slowing of the pulse by central stimulation of the vagus. The powerful vaso-constrictor and the non-toxic action of hydrastinine induced Falk to introduce hydrastinine into the treatment of haemorrhage. The following communications show that the drug has found wide recognition, especially in uterine haemorrhage.

As Falk found that the subcutaneous use of the aqueous solution of hydrastinine hydrochloride never gave rise to abscess formation, but at most to a mild burning sensation followed by infiltration which rapidly disappeared, he prescribed it subcutaneously in doses of 0.05 to 0.1 grammes ( $\frac{3}{4}$ — $1\frac{1}{2}$  grains). His prescription reads:

Rp. Hydrastinin. hydrochl. 1.0 gramm (15 grains)

Aq. destill. 10.0 grammes (170 min.)

M. Sig.:  $\frac{1}{2}$  to 1 syringeful to be injected.

He employed this medication with very good results in uterine haemorrhage due to endometritis or myomata. It proved of special value in congestive dysmenorrhœa and in too profuse menstrual loss due to tissue changes in the uterus. In the latter case treatment should be begun 6 to 8 days before menstruation is expected, half a syringeful being injected daily. When bleeding commences, one syringeful is injected every day until it has totally ceased. In irregular haemorrhages Falk injected half a syringeful 2 to 3 times a week. The employment of hydrastinine proved of less value in haemorrhage due to chronic metritis. The author never observed secondary effects, even after doses of 0.15 gramm (2 $\frac{1}{3}$  grains).

Soon after the publication of Falk's communication, A. Czempin showed that the more convenient internal administration of hydrastinine was a most efficacious measure. In his experience, it is indicated in all cases in which congestion

Falk, Archiv für Gynäkologie, Vol. 37, p. 295. — Therapeutische Monatshefte 1890, p. 19. — Merck's Bericht 1889, p. 42. — Virchows Archiv, Vol. 119, No. 3, p. 393.

Czempin, Zentralblatt für Gynäkologie 1891, No. 45, p. 905. — Merck's Bericht 1891, p. 46.

has been caused in a healthy uterine mucous membrane by disturbances of the functions of the ovaries, as for example in climacteric haemorrhage and in the haemorrhage of virgins, thereby giving rise to menorrhagia and to metrorrhagia. It should also be used in those cases in which chronic catarrhal disease of the uterine mucous membrane gives rise to a tendency to severe menstrual or atypical haemorrhages. Czempin prescribed hydrastinine as follows:

Rp. Hydrastinin. hydrochl. 0.025 gramm (2/5 grain)  
Sacchar. 1.0        " (15 grains)  
M. Ft. pulv. Mitte xij in capsul. gelatin.

Four to five doses are given daily during the first 2 to 3 days of the haemorrhage.

P. Strassmann, who carried out experiments with hydrastinine in the Women's Hospital in Giessen, confirmed the great value of the drug when administered subcutaneously or internally; he found that the preparation frequently improved the appetite, and never gave rise to unpleasant secondary effects. In one case the author gave 4.15 grammes (63 grains) of hydrastinine internally in the course of 34 days without harm. It displayed a prompt action, for haemorrhage which had been present for some time was checked after 2 to 3 days' treatment; and it was lasting, for it usually affected the following menstruation, postponing it for several days and rendering it less severe. Hydrastinine also proved of value in haemorrhage occurring in the week following curettage; and it appears to have a beneficial action, at any rate indirectly, by causing contraction of the vessels, in incomplete involution of the uterus. The author also found a decrease in the size of myomata treated by hydrastinine. In 3 cases the preparation failed either completely or partially. These were, according to Strassmann, a patient with tuberculous peritonitis and salpingitis, a patient with a placental polypus, and a hysterical person, who had been several times treated in vain, both surgically and medically, for menorrhagia. Hydrastinine deserves special consideration in the treatment of haemorrhage occurring during pregnancy, as it does not give rise to labour pains. This is confirmed by P. Baum m, who

Strassmann, Deutsche medizinische Wochenschrift 1891, No. 47,  
p. 1283.

Baumm, Therapeutische Monatshefte 1891, No. 12, p. 608.

obtained as favourable results as did Falk in gynaecological cases. But in atonic haemorrhage in the third stage of labour, hydrastinine, according to Baumm, is not more serviceable than are the preparations of ergot.

Emanuel did not adopt the prophylactic employment of hydrastinine, but tried to establish its value in menstrual haemorrhage with more certainty. He therefore only prescribed it when menstruation had become atypical on account of the intensity or duration of the bleeding, or when uterine haemorrhage occurred apart from menstruation. He always administered it by mouth in the form of gelatin perles containing 0.025 gramm (2/5 grain) of hydrastinine hydrochloride. Four of these were given during the day. Eight to twelve perles generally sufficed to check the bleeding. If this amount did not succeed, further medication was useless. The effect of hydrastinine was particularly favourable in haemorrhages due to endometritis, and it was also satisfactory in haemorrhage due to diseases of the adnexa. But in haemorrhage associated with myomata the result was negative, probably because the drug was not administered for a sufficiently long period.

Even if uterine haemorrhage may be considered the chief field for hydrastinine treatment, as appears from recent publications by H. Freund, F. Merkel, K. Lehmann, C. Credé-Hörder, R. Ziegenspeck and P. P. Laidlaw, there are also other indications for the employment of hydrastinine, e. g., haemoptysis, haematemesis, epistaxis, haemorrhoids, epilepsy and arterio-sclerosis.

Hausmann recommends it in cases of pulmonary haemorrhage in which atropine is contra-indicated. He administered 0.025 gramm (2/5 grain) 3 to 4 times a day until bleeding had ceased, and then gave a dose of 0.025 gramm (2/5 grain) once daily for 8 to 14 days.

Emanuel, Therapeutische Monatshefte 1891, No. 12, p. 613.

Freund, Therapeutische Monatshefte 1912, No. 6, p. 432.

Merkel, Münchener medizinische Wochenschrift 1912, No. 35, p. 1934.

Lehmann, Allgemeine medizinische Zentral-Zeitung 1912, No. 39, p. 512.

Hörder, Deutsche medizinische Wochenschrift 1912, No. 39, p. 1839.

Ziegenspeck, Medizinische Klinik 1912, No. 43, p. 1742.

Laidlaw, British Medical Journal 1910, II, p. 1599.

Hausmann, Therapeutische Monatshefte 1892, No. 12, p. 682. —

Medizinisch-chirurgische Rundschau 1892, No. 22.

According to P. J. Arkhangelsky and V. G. Kiseleff, hydrastinine also has a favourable influence on the course of the disease in epilepsy, as it diminishes the irritability of the cerebral cortex. The authors administered it internally in aqueous solution in doses of 0·01 to 0·02 grammes ( $\frac{1}{6}$ — $\frac{1}{3}$  grain), and daily doses of 0·05 to 0·1 grammes ( $\frac{3}{4}$ — $1\frac{1}{2}$  grains), and in the course of 2 to 3 weeks obtained a marked decrease in the number and severity of the attacks. They prescribe:

Rp. Hydrastinin. hydrochl.	2·0 grammes (30 grains)
Aq. cinnam.	25·0     ,,     ( $\frac{5}{6}$ oz)

M. Sig.: 5 drops to be taken on sugar 5 times a day.

Hydrastinine, according to Boix, is of service in cardiac disease. On account of its mild and lasting action as an arterial constrictor, its employment is specially indicated in acute and chronic aortitis and in arterio-sclerosis. In order to bring about a slow and lasting, but not an immediate, influence on the morbid process, the following mixture may be administered internally:

Rp. Hydrastinin. hydrochl.	0·1 grammme ( $1\frac{1}{2}$ grains)
Sod. iodid.	2·5 grammes (40     ,,     )
Aq. anis.	100·0     ,,     ( $3\frac{1}{3}$ oz)
Aq. destill.	150·0     ,,     (5 oz)
Syrup.	50·0     ,,     (2 oz)

M. Sig.: 2 tablespoonfuls to be taken every morning.

These doses may be increased as required. If a rapid action is required, a subcutaneous injection of half to one syringeful of the 10 p. c. aqueous solution is given twice a day.

A combination of hydrastinine and strychnine was used by W. J. Robinson in atony of the bladder. Of the following solution:

Rp. Hydrastinin. hydrochl.	0·6 grammme (9 grains)
Strychnin. sulph.	0·06     ,,     (1 grain)
Solut. aquos. saturat.	
Acidi borici min.	400

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Arkhangelsky, Dissertation Petersburg 1892. — Merck's Bericht 1892, p. 74.

Kiseleff, Russky Vratch 1892, No. 20.

Boix, Journal de médecine et de chirurgie pratique 1900, No. 19.

Robinson, Semaine médicale 1907, No. 3, p. 34. — Merck's Report 1907, p. 132.

he injected 4 drops (corresponding to 0.006 grammes ( $\frac{1}{10}$  grain) of hydrastinine and 0.0006 grammes ( $\frac{1}{100}$  grain) of strychnine) into the bladder, e. g., only a tenth of the dose of strychnine which is usually administered internally. Nevertheless, he arrived at the same result, while by this method of administration he avoided the secondary effects of internal strychnine medication (headache, diarrhoea and increased irritability). The author finds that two instillations a week are sufficient.

According to the reports of the authors mentioned above, hydrastinine is a drug which deserves the full consideration of physicians and clinicians. Besides supplying it in substance, I also issue it in the form of tablets and gelatin perles containing 0.025 grammes ( $\frac{2}{5}$  grain).

### Hydrazine Sulphate.

Hydrazine sulphate ( $\text{NH}_2 \cdot \text{NH}_2 \cdot \text{H}_2\text{SO}_4$ ), which has been employed for a variety of purposes in analysis, may serve, as suggested by Hemendra Kumar Sen and Biman Bihary Dey, for the detection of nitric acid in the presence of a large amount of nitrous acid. The authors found that hydrazine sulphate is decomposed by nitrites, forming nitrogen, nitrous oxide and ammonia, whereas no interaction occurs between nitrates and hydrazine sulphate. After the nitrous acid has been decomposed, the presence of nitric acid can be demonstrated in the usual way by means of diphenylamine. According to the authors, this process has the advantage over former processes that the nitrous acid does not require to be set free by the addition of any other acid, because the sulphuric acid, which is combined with the hydrazine, supplies the acid necessary for the decomposition of the nitrite into nitrous acid. Also, the conversion takes place so rapidly that no nitrous acid can be oxidised into nitric acid. For this reason the method is said to be superior to the well known urea method. For details of the process reference should be made to the original paper.

### Hydrochloric Acid.

A. C. Croftan has once more pointed out the value of hydrochloric acid in the treatment of pernicious anaemia.

Sen-Dey, Zeitschrift für anorganische Chemie 1912, Vol. 74, p. 52.  
Croftan, Deutsche medizinische Wochenschrift 1912, No. 51, p. 2411.  
— Compare also Merck's Report 1911, p. 265.

Since his first publication, he has further studied the action of hydrochloric acid, and has found that only those cases which are accompanied by achylia or by a high degree of hyperchlorhydria are benefited by hydrochloric acid medication. In the anamnesis, digestive disturbances always occur long before anaemia, so that a causal rôle is attributed to the gastric disturbances. The hydrochloric acid supplies the organism with an important physiological secretion, which is either absent or much diminished. Thus the nutrition of the patients is improved, and with it their resistive power and their capacity for regeneration. According to the author, the rapid disappearance of troublesome diarrhoea, which remains unaffected by other drugs, is especially striking. Croftan administered 15 drops of strong hydrochloric acid in raspberry syrup or in mucilage of acacia 6 times a day, 15 and 30 minutes after the three chief meals. This medication never caused any inconvenience. The author also prescribed a definite diet, poor in fat and excluding fresh fruit and raw vegetables. This simple and harmless method should at least be tried as a last resource in desperate cases. When changes have already occurred in the spinal cord, nothing can be expected from the treatment described. In about half the cases the author obtained no improvement, for which he is unable to offer any explanation.

### Hydropyrin.

L. Roth, like other authors, found that hydropyrin (lithium acetyl-salicylate) did not exert the slightest injurious effect either on the heart or the respiratory organs. It proved a promptly acting antipyretic, which quickly lowers the temperature and reduces the pulse rate. As an antineuralgic it was beneficial in intercostal neuralgia, cephalgia and arthritis, when given once or several times a day in doses of 1 gramm (15 grains). The author draws special attention to the anti-rheumatic action of the drug shown in acute articular rheumatism, muscular rheumatism and lumbago. R. Blum comes to the same conclusion, but in his opinion the action of hydropyrin in neuralgia is variable. While in some cases the pain rapidly disappeared and did not return, in other

Roth, Medizinische Klinik 1912, No. 3, p. 107.

Blum, Zentralblatt für die gesamte Therapie 1912, No. 7, p. 339.

cases, the action, though definite, was insufficient. In one case of neuralgia in a syphilitic subject it failed completely. On the other hand, the preparation was efficacious in fever due to phthisis, influenza and bronchitis of measles. In a few cases of pleurisy the exudate was so rapidly absorbed under the influence of hydropyrin that puncture became unnecessary. Its effect on diuresis was evident in cystitis, in which 2 to 3 daily doses of 1 gramm (15 grains) cleared the urine.

According to J. Burger, hydropyrin, while displaying a satisfactory salicylate action, gives rise to slighter secondary effects than any of the other newer preparations of salicylic acid. In his opinion, its therapeutic action is equivalent to that of aspirin. Hydropyrin has an injurious effect on the kidneys only when given in large doses and for a prolonged period, but these secondary effects are slight and soon disappear. For this reason A. Hirschberg prescribed it in gynaecological practice, in which, besides the so-called "columnisation", it gave satisfactory results in subacute pelvic cellulitis, salpingitis, oophoritis and parametritis. Hydropyrin treatment was also beneficial in dysmenorrhœa, and in nervous pains without a pathological cause.

W. Nieveling suggests the following pills to bring about "permanent antipyresis" in pulmonary tuberculosis:

Rp. Acid. arsen.	0·03 gramm ( $\frac{1}{2}$ grain)
Hydropyrin.	10·0 grammes (150 grains)
Mass pilul. q. s. ut f. pil. No. 100.	

The author prescribed 3 or 4 of these pills to be taken separately in the course of 1 to  $1\frac{1}{2}$  hours after meals, 3 times a day. If the cough was troublesome, he added 5 grammes (75 grains) of Dover's powder for every 100 pills; or other additions may be made according to the symptoms present, for example 5 grammes (75 grains) of quinine or 0·3 gramm (5 grains) of morphine. The pills were well tolerated and led in most cases to a permanent fall of temperature. To attain this effect, 250 pills were, on an average, required.

Burger, Dissertation Giessen 1912.

Hirschberg, Berliner klinische Wochenschrift 1912, No. 23, p. 1090.  
Nieveling, Deutsche medizinische Wochenschrift 1912, No. 50, p. 2359.

### Hydroquinine.

As the investigations of Morgenroth and Halberstädter had shown hydroquinine to be superior to quinine in the treatment of trypanosomiasis, it was of interest to ascertain whether hydroquinine was also more efficacious in malaria. This indeed appears to be the case. According to Giemsa and Werner, this preparation is a specific against malaria, and is more efficacious than quinine without being more toxic. Hydroquinine is not decomposed to such a great extent in the organism, for while 50 p. c. of the quinine taken is excreted in the urine, 70 p. c. of hydroquinine is excreted. Further, smaller doses are required, so that prophylaxis can be more guardedly carried out. A dose of only 0.2 gramm (3 grains) of hydroquinine is said to exert a prompt anti-parasitic action, which is plainly evident after internal or subcutaneous application. The authors administered 0.6 to 0.8 gramm (9—12 grains) a day internally in separate doses of 0.2 gramm (3 grains). Experiments with intravenous application showed that 0.75 gramm (11 grains) of hydroquinine produced the same effect as 1 gramm (15 grains) of quinine. Thus hydroquinine represents a very efficacious drug for the treatment and prophylaxis of malaria.

R. Lenzmann assumes that the spasmodic attacks in whooping-cough are caused by bacterial toxins, which stimulate the reflex arcs passing through the laryngeus. In order to mitigate this irritability he tried injections of hydroquinine, which gave admirable results. He prescribed a solution of 1 gramm of hydroquinine hydrochloride in 10 c. c. of normal saline solution, of which adults were given a daily dose of 2.5 c. c. for 4 days, and children, according to their age, were given an intravenous injection of 0.05 to 0.2 gramm ( $\frac{3}{4}$ —3 grains). Or children may be given an intramuscular injection of 0.2 gramm (3 grains) if intravenous injection should present difficulties. From the fourth day onwards the injections are given on alternate days. The author states that by the tenth day the attacks are completely checked.

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Morgenroth-Halberstädter, Merck's Report 1911.

Giemsa-Werner, Beiheft zum Archiv für Schiffs- und Tropenhygiene 1912, No. 4. — Zentralblatt für die gesamte Therapie 1912, No. 9, p. 492.

Lenzmann, Münchener medizinische Wochenschrift 1912, No. 40, p. 2193.

Experiments carried out by Morgenroth and Ginsberg on rabbits' eyes showed that the aqueous solution of hydroquinine hydrochloride, and the oily solution of hydroquinine give rise to powerful and lasting anaesthesia. Further experiments must show whether the preparation will prove a useful anaesthetic in ophthalmic practice.

### Ichthoform.

As the result of trials in typhoid fever and intestinal catarrh, H. Haller considers ichthoform\*) to be one of the best intestinal antiseptics. He treated over 30 cases of typhoid with the drug, and these showed the striking symptom that after ichthoform medication the temperature always fell slowly and steadily from at latest the third day onwards, while no relapse occurred. As a rule the patients were afebrile as early as the second week and only exceptionally as late as the third week. A happy circumstance was that in every case the patient's mind remained clear and only slight headache occurred. The course of the disease and the period of convalescence were shortened. In the early stage cases of typhoid could be completely cut short, even severe cases commencing treatment with temperatures of 40° and 41° C. Ichthoform was administered to adults in doses of 0.5 gramm (7½ grains), given from 3 times a day to once every three hours, according to the severity of the case and the number of stools. In severe cases it was given every three hours combined with 0.05 gramm (¾ grain) of opium and 0.05 gramm (¾ grain) of calomel. This treatment caused a considerable reduction of the stools. If constipation resulted, the opium was omitted. The author also obtained good results, at least in milder cases, with 0.3 gramm (5 grains) of ichthoform and 0.2 gramm (3 grains) of purified sulphur. Besides the medication described, cold compresses were applied to the abdomen and chest in cases with high temperatures. Ichthoform also gave satisfactory results in intestinal catarrh not associated with tuberculosis.

Morgenroth-Ginsberg, Berliner klinische Wochenschrift 1912, No. 46,  
p. 2184.

Haller, Therapie der Gegenwart 1912, No. 11, p. 525.

\*) Compare Merck's Reports 1899—1903.

**Ichthynat.**

H. Oppenheim tested ichthynat\*) thoroughly in gynaecological practice, chiefly in non-suppurative acute and subacute inflammation of the adnexa, in serous perimetritis and parametritis exudates and in various inflammatory affections of the uterine mucous membrane. For suppurative processes of the internal genital organs, operative measures are, according to the author, required; nor is ichthynat indicated for infective purulent inflammation of the endometrium, the vagina, vulva and urethra. Apart from these cases, ichthynat is of great service in a large variety of inflammatory affections of the genital tract.

The author draws special attention to the analgesic action of ichthynat. By the use of 20 p. c. ichthynat-glycerin in the form of tampons, even the severe pain of peracute oöphoritis was alleviated or allayed after two or three applications. Care must be taken that the tampons are sufficiently large, that they are well soaked with the medicament and that they are correctly placed. To this end the author offers a number of suggestions.

A further advantage of ichthynat lies in its absorptive power and its property of counteracting inflammation, besides which it causes anaemia, acts as a reducing agent, a desiccator and astringent, without in any way irritating the mucous membranes. The therapeutic effect of the drug may be increased by its simultaneous internal administration. For this purpose ichthynat-gelatin capsules are employed, containing 0.15 gramme ( $2\frac{1}{3}$  grains) of ichthynat. Two of these are given 3 to 4 times a day after meals. The internal medication is only omitted in the case of weak stomachs in order to avoid troublesome gastro-intestinal symptoms. In Oppenheim's experience, ichthynat treatment may be specially recommended in acute and subacute salpingo-oöphoritis, in parametritis and perimetritis and in metro-endometritis. Bacterial purulent processes, especially gonorrhœal processes, are excluded from treatment, as are all chronic diseases of the genital tract which are accompanied by fibrous adhesions or by cystic degenerative changes.

\*) Compare Merck's Report 1907.

\*Oppenheim, Deutsche medizinische Wochenschrift 1912, No. 45, p. 2126.

**Ichthyol.**

As I have previously reported, ichthyol forms an excellent application for wounds\*). This has recently been confirmed by W. N. Domarew, who used 10 p. c. ichthyol-glycerin for surgical purposes in 150 cases. In a number of wounds, in which cleansing and the application of aseptic dressings did not bring about the desired result, as suppuration continued and the process of healing was prolonged, he obtained rapid and satisfactory results by the use of ichthyol-glycerin. The action of the drug was apparent by a diminution in the secretion from the wound, the disappearance of the suppurative character of the wound and the promotion of granulation formation. It is due to the disinfectant, astringent and mildly irritative property of 10 p. c. ichthyol-glycerin, the glycerin not merely playing the part of a simple vehicle, but assisting the action of the ichthyol. The disappearance of inflammatory symptoms and the relief from pain caused by ichthyol are noteworthy. These make manifest the resolving and analgesic properties of ichthyol. Ichthyol, in the concentration mentioned, has no keratoplastic action, but its stimulant action makes it possible to discontinue the application of ichthyol-glycerin as soon as the wound has filled up and keratoplastic closing is required. A simple dry aseptic dressing is all that is necessary.

J. Allert obtained very satisfactory results in a number of skin diseases. Among children ichthyol proved useful in a number of cases of impetigo contagiosa, in which dressings with a 2 to 5 p. c. ichthyol solution, or inunction with 5 to 10 p. c. ichthyol ointment, always acted promptly, healing existing lesions and preventing the development of fresh eruptions. The results of ichthyol treatment were also excellent in herpes tonsurans and sycosis parasitaria. After loosening the scales and scabs by means of oil, the affected parts were painted with pure ichthyol and a powder applied. When the epidermal crusts have come away, a 10 p. c. ichthyol ointment is applied until the skin has attained its normal character. Ichthyol has the advantage over tar, chrysarobin, lenigallol, etc., that it may be applied to extensive

\*) Compare my previous Reports.

Domarew, Deutsche Medizinalzeitung 1912, No. 26, p. 485.

Allert, Deutsche Ärzte-Zeitung 1912, No. 15.

areas of diseased skin without danger of poisoning. In eczema marginatum ichthylol is useful if the affected cutaneous areas are cleansed with spirit of soap, ichthylol energetically painted on and the patient wrapped up. This procedure is at first carried out daily, and then on alternate days, and by its means a cure is effected. Towards the end of treatment ordinary zinc ointment is applied until the skin has returned to its original suppleness.

The author also obtained a prompt action with ichthylol in pityriasis versicolor. In his experience, the painting should be thorough and complete in these cases to prevent relapse. An equally good result was obtained by the author in a case of pityriasis rosée (Gilbert). But painting with pure ichthylol in an extensive and exceedingly obstinate case of erythrasma did not effect a complete cure, which was only obtained following energetic treatment with 20 p. c. ichthylol ointment.

Ichthylol treatment in pulmonary tuberculosis is discussed by W. Odell and R. Weissmann. A direct action of the drug on the disease germs is excluded by previous experiences with ichthylol; but the results obtained by the authors mentioned above show that the preparation improves nutrition, retards the consumption of albumin, stimulates digestion, increases the appetite and thus improves the general condition of the patient and his resistive power. Ichthylol is a reducing agent and acts upon the tissue as an antiphlogistic, an analgesic and an antiseptic. Odell further points out that ichthylol lowers the temperature and keeps its variations within close bounds. The author began with 3 daily doses of 5 drops, gradually increasing the dose to 10 drops, and prescribed malt and cod-liver oil as well. In private practice he sometimes prescribed iron-ichthylol tablets also. His results in 189 cases are as follows: The disease was brought to a standstill in 43 cases, was very considerably improved in 83 cases, considerably improved in 18 cases, improved in 27, remained stationary in 6 cases; 11 cases were unsuitable and 1 patient died. This result compares favourably with those obtained by other methods of treatment. Weissmann arrived at similar conclusions; he states that he has

had wide experience with ichthyol. He considers ichthyol more efficacious than its substitutes.

### Insipin.

This new preparation of quinine\*) has been thoroughly investigated by U. Silva. Therapeutically it has proved completely successful, both as regards its facility of application, which presents no difficulties on account of its slight taste, and as regards its results. No disturbances or irritative symptoms were ever observed in connection with the digestive organs. Even when given immediately after meals, the drug did not cause nausea or vomiting, although the author gave daily doses up to 2 grammes (30 grains) for a prolonged period. Nor did symptoms of quinine intoxication occur, or only to a slight degree, and these were easily avoided, however, even in patients who showed great sensitiveness in hearing following the use of other preparations of quinine. The therapeutic effect was evident in typhoid, malaria and the evening rise of temperature of phthisical patients. In typhoid the temperature rapidly fell by about 1° C., in malaria correct administration of the drug checked the fever, and the fever of tuberculosis decreased in intensity and duration, while the sweats were abolished. As the author attached more importance in typhoid to the cardio-vascular than to the antipyretic action, he kept the dosage under 1 gramme (15 grains) of insipin, in tuberculosis he gave 1 to 1.2 grammes (15—18 grains), and in malaria 1.5 to 2 grammes (24—30 grains), 2 to 3 hours before the attack during the first days.

Silva paid special attention to the influence of insipin on the activity of the organs and on metabolism. The preparation is rapidly absorbed and its presence in the urine can be demonstrated 10 minutes after ingestion. Its complete excretion, however, takes longer than is the case with quinine sulphate. The author considers this to be the reason of its greater efficacy. He further found that insipin retards oxidation in the organism and decreases metabolism, but to a less degree than other quinine salts. Its slighter effect on metabolism is advantageous, because in prolonged cures the administration of insipin need not be interrupted.

\*) Compare Merck's Report 1911.  
Silva, II Cesalpino 1912, No. 4.

The action of insipin on the blood consists in an increase in the red blood corpuscles and in the haemoglobin content; its action on the circulatory apparatus in typhoid consists in the strengthening of cardiac activity. The size of the heart remained unaltered. The ventricular systole became stronger, the blood pressure rose, the pulse rate was lowered and regulated and in a few cases dicrotism was diminished. Insipin is therefore also a cardiac tonic.

### Inulin.

Inulin, a form of starch occurring in various Composites, as for example in the roots of elecampane and Jerusalem artichoke, has been tried by various observers for the carbohydrate nutrition of diabetics, but opinion regarding its value is divided. After Külz had recommended it, it was rejected by Naunyn and Socin. Lewis, as the result of his experiments, concluded that it could not be used as a source of energy for diabetics. He believes that the drug is only rendered useful when it is sufficiently hydrolysed, which is only effected by its remaining for a long time in the acid gastric juice. He states that it undergoes no alteration in the intestine and that it is probably excreted by the organism in an unaltered state. H. Strauss has, on the other hand, recently expressed himself in favour of inulin. He carried out experiments in a number of severe and fairly severe cases of diabetes mellitus, the results of which appear entirely to confirm his recommendation. With regulated diet the administration of 100 grammes ( $3\frac{1}{3}$  oz) of inulin a day only led to a slightly increased excretion of sugar, as compared with the previous period of carbohydrate-free diet, and it exercised a distinctly favourable influence on acetonuria. Inulin was very well tolerated. The patients did not lose weight during inulin treatment, but rather gained in weight and there was no evidence that tolerance was affected, as Socin assumed to be the case. Of 11 patients, only two complained of slight gastric trouble at the conclusion of treatment, apart from which there were no complaints. In no case was there any evidence of intestinal trouble.

Lewis, Journal of the American Medical Association, April 20, 1912,  
Zentralblatt für die gesamte Therapie 1912, No. 10, p. 513.

Strauss, Deutsche medizinische Wochenschrift 1912, No. 10, p. 441.  
— Berliner klinische Wochenschrift 1912, No. 26, p. 1213.

Comparative tests with oatmeal and wheatmeal soups showed that inulin was in every case better or just as well tolerated as these. With regard to the slight capacity of the intestine for absorbing inulin, which has been referred to above, it does not appear to differ considerably from that of other forms of starch. In the absence of gastric subacidity, according to the results of Strauss' investigations, inulin, like other forms of starch, is converted into lactulose and absorbed. The circumstance that the prolonged administration of large quantities of inulin usually exerted an unmistakable influence on acidosis is in favour of this view. The author therefore feels justified in recommending the administration of inulin in diabetes as a beneficial procedure, superior to oatmeal and wheatmeal cures.

### Iodic Acid.

Schiele found iodic acid, the value of which as a disinfectant is well known\*), to be a useful drug in the treatment of trachoma. J. Rudas investigated the statements of the author mentioned, and was able to confirm them fully. According to his prescription, iodic acid is used in the form of little pencils which are prepared by adding gum acacia and water, and, if necessary, acoine. In a large number of cases, the author compared the results of iodic acid treatment with those obtained by other methods of treatment, and found the iodic acid treatment of trachoma to be far superior to the customary methods. A cure generally took place 20 days earlier. The treatment consists in getting rid of inflammatory symptoms, anaesthetising by means of cocaine hydrochloride, cauterising with the iodic acid pencil and finally treating with a 3 p. c. boric acid solution.

### Iodine.

During the past year various authors have discussed the value of iodine in skin diseases and infective diseases. Cavazzani found iodine very useful in Malta fever and in

Schiele, Zentralblatt für praktische Augenheilkunde 1900, p. 97. —  
Merck's Report 1900, p. 43.

\*) Compare Merck's Report 1905.

Rudas, Archiv für Augenheilkunde 1912, Vol. 72, p. 51. — Wochenschrift für Therapie und Hygiene des Auges 1912, Vol. 16, p. 5.  
Cavazzani, Gazette médicale de Paris 1912, p. 289. — Klinisch-therapeutische Wochenschrift 1912, p. 924.

Bacillus coli infections, and especially in pertussis, but he is of opinion that it is of no value in acute pneumonia and broncho-pneumonia, in scarlet fever, measles, erysipelas and acute articular rheumatism. In pertussis he prescribed a solution of 1 gramme (15 grains) of iodine and 15 grammes ( $\frac{1}{2}$  oz) of potassium iodide in 15 grammes ( $\frac{1}{2}$  oz) of water, of which he gave 4 to 6 drops a day to children one year old, 6 to 10 drops to children of 2 to 5 years, and 10 to 15 drops to older children, in milk or coffee. If this medication is commenced early, the disease runs a favourable course; it alleviates the cough, guards against complications and shortens the duration of the illness. It is said to give rise to no unwelcome sequelæ and can readily be combined with quinine and bromine-camphor.

In contradistinction to Cavazzani's experience, Binet also obtained good results with external iodine treatment in erysipelas. Painting with tincture of iodine rapidly reduced the fever, in 3 to 4 days the swellings subsided and in about 5 days desquamation took place. Rockhill obtained equally good results in variola by painting with iodine. He used a 10 p. c. solution of iodine in glycerin, and had no failures among 85 cases. The pustules healed rapidly and the cosmetic result was highly satisfactory.

Consoli administered tincture of iodine by mouth and rectally in cholera. He gave 300 c. c. a day of a mixture of 50 drops of tincture of iodine and 1 litre of water. For intestinal irrigation he prescribed the same mixture in amounts of 1 litre, at a temperature of 37 to 40° C. In the patients so treated the vomiting ceased, the diarrhoea was diminished, the pains were alleviated and the general condition was improved. The mortality amounted to 37 p. c.

G. Farnarier describes an original method of disinfecting the bladder. It consists in the application of iodine vapour to the bladder by means of a special apparatus. The iodine vapour is produced by heating iodoform (0.05 gramme) and is allowed to remain for about 5 minutes in the bladder, which has been previously emptied. In 17 cases of cystitis, the author cured 2 cases by means of this treatment, while

Binet, Provence médicale 1912, No. 21.

Rockhill, Journal of the American Medical Association 1912, No. 4.

Consoli, Journal de pharmacie et de chimie 1912, II, p. 137.

Farnarier, Semaine médicale 1912, No. 28, p. 326.

the remaining cases were improved. In only one case did the patient complain of pain. Even a case of post-gonorrhœal cystitis was cured after 7 fumigations with iodine, carried out at intervals of 4 to 5 days.

P. Moiroud applied iodine fumigation with success to syphilitic ulcers. He conducted iodine vapour in a suitable manner over phagedenic soft sores; by this treatment the infiltrations and the offensive odour disappeared and the wound surface became clean. Iodine should be applied twice a day at first and should be discontinued immediately the healing over and cicatrisation of the ulcer has begun. Occasionally the iodine causes pain lasting for a few minutes.

A. Hofmann reports four cases of tuberculous peritonitis, in which very good results were obtained by painting the peritoneum with iodine after the operation. Healing took place rapidly and proved to be permanent on subsequent examination. No injurious effect was observed following the use of a 10 p. c. tincture of iodine. Special interest is attached to the author's observation in one case, in which the iodine treatment caused the pulmonary symptoms also to subside rapidly. It is also of excellent service, according to W. Wolf, after the operative treatment of tuberculosis of bones and of soft parts, in which tincture of iodine is said to prove an almost sovereign remedy.

The communications of F. Brüning, E. Lardy, Kutschér, Vigliani and Zaffiro, Pickenbach, J. A. Dalton, Cole Madden, M. Watkins, O. Klepatski

Moiroud, *Revue internationale de médecine* 1912, No. 13, p. 240.

— *Gazette médicale de Paris* 1912, No. 13, p. 193.

Hofmann, *Münchener medizinische Wochenschrift* 1912, No. 10, p. 531.

Wolf, *Zentralblatt für Chirurgie* 1912, No. 11, p. 347.

Brüning, *Zentralblatt für Chirurgie* 1912, No. 19, p. 643.

Lardy, *Deutsche Zeitschrift für Chirurgie* 1912, Vol. 116. — Kocher, *Festschrift, Zentralblatt für Gynäkologie* 1912, No. 47, p. 1599.

Payr, *Zentralblatt für Chirurgie* 1912, No. 12, p. 386.

Kutschér, *Deutsche militärärztliche Zeitschrift* 1912, No. 5.

Vigliani-Zaffiro, *Rivista veneta di scienze mediche* 1912, Vol. 56, No. 6.

Pickenbach, *Medizinische Klinik* 1912, No. 12, p. 487.

Dalton, *British Medical Journal* 1912, II, p. 765.

Madden, *British Medical Journal* 1912, II, p. 765.

Watkins, *Surgery, Gynecology and Obstetrics* 1912, Vol. 15, No. 1.

Klepatski, *Dissertation Geneva* 1911.

and Ombrédanne are of interest in surgery. All the authors express a favourable opinion on the disinfection of the skin by iodine before operations. Brüning, on Küttner's advice, used a 5 p. c. tincture of iodine for this purpose, but after having met with a failure he returned to the 10 p. c. tincture. Ombrédanne does not consider the tincture of iodine prepared with alcohol to be suitable on account of its irritant action on the skin, and suggests in its place a solution of iodine in chloroform (1:20). With this the dry skin over the site of the operation is painted until it assumes a distinct brown coloration.

Kutscher, in opposition to Grossich, considers the action of tincture of iodine to be due not to sterilisation but to the desiccating property of alcohol and of iodine, which greatly diminishes the capacity of the skin for shedding germs. Several of the authors mentioned above, such as Pickenbach and Lardy, praise the simplicity and the efficacy of the iodine treatment of wounds. Pickenbach even obtained perfect healing of dirty wounds by painting with iodine. In his opinion, it is impossible to find anything simpler, cheaper and more rapid for the disinfection of skin and wounds. The wound area is first freed from dirt as far as possible by means of cotton wool soaked in benzin, then the entire region, including the wound itself, is thoroughly painted with tincture of iodine and covered with iodoform gauze and a dry dressing. This procedure is particularly suitable for the immediate dressing of wounds, before the patient can obtain expert assistance, as it requires no special surgical training.

Payr has for many years used tincture of iodine with success for the disinfection of the mucous membranes in operations on the stomach and intestines. In the presence of much mucous secretion covering the gastric mucous membrane, the latter was wiped dry and then energetically treated with a 5 p. c. tincture of iodine. The large intestine was cleansed in the same way by means of swabs on holders and the lumen was then painted with iodine. The method is

Ombrédanne, Klinisch-therapeutische Wochenschrift 1912, No. 44,  
p. 1304.

Küttner, Archiv für klinische Chirurgie 1911, Vol. 95, No. 1.  
Grossich, Merck's Report 1910, p. 219.

well suited for considerably diminishing the possible sources of error in aseptic operations on the gastro-intestinal tract.

Iodine, according to P. Carles, is also useful for the disinfection of the mouth. For this purpose he prescribes a solution of 1 gramme (15 grains) of potassium iodide and 2 grammes (30 grains) of iodine in 20 grammes ( $\frac{5}{6}$  oz) of alcohol (95 p. c.), of which 1 to 3 drops in a glass of water as hot as can be borne are used to rinse the mouth. If the mouth is rinsed with this solution every evening, it is said to prevent the formation of tartar.

Miller reports upon the successful treatment of a goitre in a small dog. He had it rubbed daily with an iodine ointment having the following composition: Rp. Iodi 0·5, Pot. iod., Aq. destill. aa 5·0, Adip. suill. 10·0, Adip. lan. 40·0. After 10 days a diminution of the swelling was observed. The general condition of the animal had also improved, the difficulty of respiration and the dribbling of saliva were only present to a slight degree, and the animal again took a sufficient quantity of food. After 4 weeks' treatment and the use in all of 121 grammes of the ointment, the goitre had completely disappeared and the dog remained permanently well.

### Iodipin.

H. Winternitz deals exhaustively with the present position of iodipin treatment, and discusses fully the results which have so far been obtained by the use of iodipin and gives a clear account of the value of this drug, physiologically, pharmacologically and therapeutically, compared with other iodine preparations. The author points out specially that iodipin occupies a unique position, because it can be applied subcutaneously with great benefit and without causing harm, and by this method of administration it displays a lasting and uniform iodine action. Its subcutaneous application has the additional advantage that patients are able to undergo iodine treatment who cannot tolerate iodine preparations when given by mouth. As the injection of large doses occasionally causes trouble, the author recommends, as Gorbatow did

Carles, Gazette des sciences médicales de Bordeaux 1912, 25<sup>th</sup> February. — Zentralblatt für die gesamte Therapie 1912, p. 517.

Miller, Berliner tierärztliche Wochenschrift 1912, No. 37, p. 682.

Winternitz, Therapeutscheskoje Oboshrenie 1912, No. 6 and 7.

before him, that small doses of 3 to 5 c. c. should be given in place of a single large dose, and that they should be injected more frequently. With regard to the indications for iodipin, the preparation deserves special consideration in arterio-sclerosis, as in this condition it leads to the improvement of the general health and of sleep, regulates the bowels, diminishes the anginal attacks, alleviates pain, reduces the aneurysms and diminishes the circumference of the aorta in aortic dilatation. But its chief indication is syphilis, and especially tertiary syphilis, in the treatment of which iodine has always played an important part. Iodipin is preferable to other preparations of iodine, because a constant and uniform action is obtained by its subcutaneous injection. Recently iodipin has been found of value in sepsis, puerperal infections, pyæmia, bronchopneumonia, peritonitis, erysipelas, scarlet fever, etc., in which it has a beneficial effect on the temperature and the general health.

A case which strikingly illustrates the efficacy of iodipin in septic affections is reported by Sick. The case was one of sepsis of the liver, probably due to *Coli* infection. Neither the daily high temperatures nor the severe rigors were affected by quinine or by other drugs. On the 32nd. day, after a severe rigor and a temperature of 40.4° C., the author administered 10 c. c. of iodipin (25 p. c.), whereupon the intermittent temperature fell by lysis in the course of four days. The fever returned, but again subsided promptly on treatment with iodipin. After three applications the general health had improved markedly and convalescence ensued.

M. Herz is also not in favour of large doses of iodipin. In his experience, quite small doses lead to satisfactory results, for example in cerebral arterio-sclerosis. He begins with iodipin tablets, and during the first days he prescribes one tablet after food, gradually increasing the dose up to at most 6 tablets a day. But he does not increase the amount if the smaller doses effect the disappearance of the troublesome symptoms.

C. Warfield, who has for years paid special attention to iodipin and its employment, is also in favour of the

Sick, *Münchener medizinische Wochenschrift* 1912, No. 43, p. 2370.  
Herz, *Wiener medizinische Wochenschrift* 1912, No. 8.

Warfield, Iodine used therapeutically in nose and throat affections. San Antonio 1912. (Reprint.)

administration of small doses, which have proved of special value in simple goitre and which do not give rise to iodism. By means of subcutaneous daily doses of at most 2 grammes (of the 25 p. c. preparation) he always obtained good results. Iodipin acted almost as a specific in hay fever, having a tonic effect on the mucous membrane, which is the seat of the malady. The author had not a single failure among his cases. Iodipin also acts slowly but surely in asthma and hay fever asthma, which is probably an anaphylactic symptom. This action is no doubt due to the elimination of the irritating toxin and to an increase in the resistive power of the affected mucous membranes. The treatment must be carried out for 4 to 6 months during the first year, for about 4 months during the second year, and for 2 to 3 months, if still necessary, during the third year. The positive results of iodipin treatment in atrophic rhinitis of syphilitic origin and in neuroses of the nose and pharynx may probably be explained in the same way as its use in hay fever. A trial with iodipin may also be recommended in chronic (foetid) bronchitis, as iodipin, according to the author, is the sole drug which has any influence in this disease; it brings about the elimination or absorption of the pathological secretions and causes the disappearance of the offensive odour. Its action is specially evident in the presence of old pleuritic adhesions. Warfield expects much benefit from iodipin medication in incipient pulmonary tuberculosis; in laryngeal tuberculosis, in conjunction with local antiseptics and sedatives, it is, in his experience, the best remedy.

J. F. Early discusses the treatment of asthma by iodipin. He specially emphasises the efficacy of iodipin injections, the absence of irritant action, the almost total painlessness, and constant uniform action. In a case of chronic bronchitis, however, in which the attacks of coughing were so severe that they caused a rupture, its internal administration proved highly beneficial. The attacks, which had in the course of years become asthmatic in character, were very favourably influenced by the daily administration of 4 doses of 1 teaspoonful of iodipin (10 p. c.), and the cough was completely cured.

Rumpf reports a case of chronic articular inflammation with deformity, in which he had injected 2 grammes of sterile olive oil into the knee-joints with surprisingly good results. But as the good result was only transient, he tried adding iodipin to the olive oil, in order to excite the production of synovial fluid. As a rule he used an oily mixture containing 5 p. c. of iodipin. The injection of this mixture produced a different effect. It usually caused an effusion into the joint, which might be painful for a few days, but considerably improved the mobility of the joints and the power of motion; a stiff shoulder-joint could be used after 8 to 10 days. For sensitive patients weaker solutions should be employed. Iodoform cannot be used as a substitute for iodipin, as it is very painful and does not furnish such good results.

In muscular affections due to syphilis, intramuscular injections of iodipin might prove beneficial. According to F. Gudzent, they proved very useful in a case which had previously been unsuccessfully treated by aspirin and hot air on account of severe pain in the muscles of the neck. Potassium iodide gave rise to severe iodism, but the patient tolerated well an injection of 10 c. c. of iodipin (25 p. c.) given intramuscularly at intervals of 3 to 8 days. After the first injection the pains in the muscles of the neck grew less and the patient's condition improved with each further injection. The Wassermann reaction, which had been positive, became negative. In another case, that of a syphilitic articular affection, treatment by iodipin was unsuccessful.

Finally reference may be made to the communication of Schoemaker, which confirms the statement made by Fritsch with regard to the utility of iodipin in the representation of fistulous passages by means of X rays.

### Iodipin for Veterinary Use.

The efficacy of iodipin in meningo-encephalitis, which was assumed by Mitteldorf, has been confirmed in a communication by H. Thum. According to this, the author

Rumpf, Münchener medizinische Wochenschrift 1912, No. 25, p. 1410.  
Gudzent, Charité-Annalen Vol. 25.

Schoemaker, Zentralblatt für Chirurgie 1912, No. 42.

Fritsch, Merck's Report 1911, p. 280.

Mitteldorf, Berliner tierärztliche Wochenschrift 1904, No. 7, p. 113.

Thum, Monatshefte für praktische Tierheilkunde 1912, Vol. 23, p. 71.

obtained only good results in meningitis of horses, for by the administration of iodipin even those animals recovered in which treatment was commenced late, when severe symptoms of depression already existed. Each horse was at first given a subcutaneous injection of 30 c. c. of 25 p. c. iodipin into the neck, repeated once in 2 or 3 days. After an interval of 4 days 40 c. c. were injected and this was repeated after a period of 5 days. As a final injection, after 5 to 8 days, Thum gave a dose of 60 c. c., so that a horse received altogether 200 c. c. After the second injection the symptoms of depression were diminished, the food was taken better and gradual recovery followed. The author ascribes these good results to iodipin. He frequently observed the appearance of extensive œdema at the site of injection, which was, however, absorbed without treatment and without abscess formation. This local reaction is also discussed by J. Lukas, who used iodipin with satisfactory results in horses suffering from contagious pneumonia and tetanus. He admits that in many horses local reactions may occur in the form of swelling, formation of an abscess and suppuration, but this is not the case with all horses and does not occur at every site of injection in the same animal. They either disappear without any intervention, or they consist of sterile abscesses, such as occur after the injection of sterile turpentine oil. In the author's opinion, the powerful positive chemotaxis which is present in the sterile abscesses may cause the paralysis of toxins, and this may explain the cure of tetanus and of other infective diseases. But iodipin has in this respect an advantage over turpentine oil in that it does not, like the latter, give rise to pain and restlessness.

K. Wischnewski gave to a horse, suffering from contagious pneumonia, 3 injections of 60 c. c. of iodipin at intervals of 3 days with complete success. The author also succeeded in curing mastitis in a cow by means of 5 injections of iodipin.

Kräenze observed a great improvement after the injection of 50 c. c. of iodipin in a horse which was suffering from metastatic pneumonia as a sequel to glanders, and two more injections led to a cure.

Lukas, Tierärztliches Zentralblatt 1911, No. 34.

Wischnewski, Veterinarny Wratsch 1912, No. 39.

Kräenze, Münchener tierärztliche Wochenschrift 1912, No. 35.

Lutzenberger successfully treated a horse suffering from hepatic cirrhosis. Two injections of 50 c.c. of iodipin each were followed by an improvement and food was no longer refused. Further treatment brought about a cure.

Gerasimow describes two cases of periodic ophthalmia accompanied by corneal opacity in horses, in which injections of iodipin were followed by excellent results.

#### Iodival.

A. B. Katschkatschew, who used iodival\*) in his private practice in a large number of cases requiring iodine medication, expressed a favourable opinion with regard to the efficacy of the preparation. The author points out specially that it was occasionally well tolerated in cases in which potassium iodide gave rise to gastric disturbance. The absence of troublesome secondary effects is confirmed by Reinsch. He states that definite benefit resulted from the iodival treatment of chronic atrophic foetid rhinitis, whether due to syphilis or to tuberculosis. The author never met with iodism, even after prolonged administration, or in children or debilitated patients. He prescribed 1 tablet (0.3 gramm [5 grains] of iodival) 3 times a day, and sometimes increased the dose to 2 tablets.

F. Dorn, as a result of his experiences, also regards iodival as a good substitute for potassium iodide in the treatment of arterio-sclerosis and affections of the respiratory passages.

#### Iodocitin.

The recognised efficacy of lecithin as a nerve tonic leads Chrzelitzer to assume that iodo-lecithalalbumin constitutes a suitable preparation for combining the action of lecithin with that of iodine. In tabes, scrofula, syphilis, neuralgia, general paralysis and bronchial asthma he has obtained very satisfactory results with the preparation. Jaeger pre-

Lutzenberger, ibid. 1912, No. 46.

Gerasimow, Veterinarny Wratsch 1912, No. 16.

Katschkatschew, Wratschebnaja Gazeta 1912, No. 16.

\*) Compare Merck's Report 1911.

Reinsch, Zeitschrift für ärztliche Fortbildung 1912, p. 241.

Dorn, Allgemeine medizinische Zentral-Zeitung 1912, No. 46, p. 602.

Chrzelitzer, Dermatologische Wochenschrift 1912, No. 6, p. 168.

Jaeger, Therapie der Gegenwart 1912, No. 4, p. 191.

scribed it, always with good results, in arterio-sclerosis, apoplexy, exudates, embolism and vertigo. For these cases the daily administration of 1 to 2 tablets (each containing 0·06 grammie [1 grain] of iodine) usually sufficed. The iodine action set in after a few hours and its excretion was effected in 2 to 3 days. Iodism was not observed or only occurred in a mild form. Secondary effects in connection with the stomach and intestine did not occur, but the appetite was increased with consequent rise in the body-weight.

Steiner made a careful investigation of iodocitin in arterio-sclerosis. According to the case histories reported by the author, the effects of the drug were always good. This was also the case in cerebral arterio-sclerosis, as was to be expected on account of the two principal components of iodocitin. However, according to Steiner, the preparation is not entirely free from secondary effects.

### Iodoform.

During the past year T. W. Dewar recommended intravenous injections of iodoform for the treatment of pulmonary tuberculosis; they are said to be very beneficial if applied in the early stages. The author has recently also found this treatment very efficacious in pertussis, inflammation of the lungs and pulmonary catarrh. He applied the treatment to a boy, aged 15, with the result that the cough remained severe for the first two days and then entirely disappeared in the course of 10 days. In this case he gave 10 injections, i. e., one injection a day. In other cases, also, the author was well satisfied with the results of iodoform treatment. It not only cured the cough, but also improved the general health. For each injection he used a solution of 0·06 grammie (1 grain) of iodoform in 10 times the amount of ether (sp. gr. = 0·72); if the vein was small, he added 2·5 to 20 p. c. of liquid paraffin to the mixture. But the paraffin occasionally caused shortness of breath and increased the cough. The method presents difficulties in small children, in whom injection is difficult on account of the small size of the

Steiner, Deutsche medizinische Wochenschrift 1912, No. 29, p. 1317.  
Dewar, British Medical Journal 1912, II, p. 681. — Compare  
Glasgow Medical Journal 1911, p. 7 and Merck's Report 1911,  
p. 283.

veins. Dewar does not, therefore, advise its employment in children.

The good results of iodoform injections in pulmonary tuberculosis are confirmed by W. M. Crofton and Higgins. The latter carried out experiments on rabbits infected with tuberculosis and found that iodoform injections gave rise to an increase in weight and, as was shown at the autopsy of the killed animals, promoted the production of fresh connective tissue in place of the affected pulmonary tissue. Crofton describes two cases of miliary tuberculosis which were cured by the above treatment. While Dewar attributes the action to the splitting up of iodoform in the organism into iodine and formaldehyde, Crofton considers it to be due to the conversion of toxins into toxoids by the iodoform. G. Holz points out that iodoform (like iodine in any form) brings about a considerable increase in lymphocytes. As this lymphocytosis persists for a very long time, the author considers that herein may be found the explanation of the action of iodoform. Hotz also considers the action of iodine to be essentially due to lymphocytosis.

New experiences with the Mosetig-Moorhof iodoform bone plugs are reported by A. Wettstein and F. Schulze. According to Wettstein, the iodoform plug (mixture of 4 parts of iodoform, 3 parts of sesame oil and 3 parts of spermaceti, compare Merck's Reports 1903, 1904, 1905) presents a means by which the tedious process of healing of chronic infective and tuberculous osteomyelitis may be considerably shortened and unsightly scars avoided. Schulze also obtained very good results with this plug. He employed it for bony cavities, depressed abscesses, fistulas leading into joints, osteomyelitis, resections of tuberculous foci and arthritis deformans. It is of great benefit in cases of large sequestra. A wide opening must be made and after having been plugged must be sown up in layers. Iodoform fistulas occurred several times after the operation, but never suppuration. The author therefore

Crofton-Higgins, British Medical Journal 1912, I, p. 294.

Holz, Mitteilungen aus den Grenzgebieten der Medizin und Chirurgie 1912, Vol. 25, p. 100.

Hotz, Deutsche medizinische Wochenschrift 1912, No. 51, p. 2438.

Wettstein, Medizinische Klinik 1912, No. 6, p. 240.

Schulze, Münchener medizinische Wochenschrift 1912, No. 43, p. 2365.

draws the conclusion that iodoform influences the suppuration and shortens the process of healing.

Working on the hypothesis that foot and mouth disease spreads not only by way of the digestive organs, but is carried in the air by way of the respiratory organs, Leneveu and Gosselin have suggested treating cattle by means of iodoform in order to guard against infection. When the animals are attacked by the epidemic when grazing, they are brought into the sheds and 5 c. c. of a saturated ethereal solution of iodoform is poured into the nostrils 3 times a day. Young animals are given only a third to two-thirds of this dose. In animals which show no aphthæ treatment is discontinued on the fifth day. It is renewed if aphthæ appear. If aphthæ are present the treatment is continued for 6 days. Supplementary treatment is not required, but aperients should be administered.

#### Iodoglidine.\*)

The iodine treatment of pulmonary tuberculosis is, according to Nieveling, of marked advantage, even though it can never take the place of other medicaments or of general treatment. In almost every case it acts as an expectorant, has a beneficial effect on shortness of breath, strengthens the cardiac action, thus getting rid of palpitation, favours the cicatrisation and induration of tuberculous foci in the lungs, or at any rate delays the breaking down of tuberculous tissue. It does not, however, affect the temperature. The iodine preparation used by him was iodoglidine, of which he prescribed 1 tablet 3 times a day.

M. Alexander prescribed iodoglidine in a variety of diseases in which iodine is indicated, especially for patients having weak stomachs, as in his experience the preparation has no secondary effects on the stomach or intestines. G. Flatau also used it with success in similar cases.

Leneveu-Gosselin, Berliner tierärztliche Wochenschrift 1912, No. 15,  
p. 267.

\*) Compare Merck's Report 1911.

Nieveling, Berliner klinische Wochenschrift 1912, No. 42, p. 1973.

Alexander, Fortschritte der Medizin 1912, No. 46.

Flatau, Fortschritte der Medizin 1912, No. 16.

**Iodostarin.**

In a variety of eye diseases, such as affections of the retina and choroid, of the vitreous humour and the cornea, in which preparations of iodine are usually given, Beck prescribed iodostarin\*), directing his attention more especially to the manner in which the preparation was tolerated when given in daily doses of 1 to 3 grammes (15—45 grains) for a prolonged period. In one case only he observed unilateral headache on the day following the administration of the first dose. As this persisted on leaving off the drug, the author does not attribute it to the medicament. In another case slight signs of iodism occurred. Otherwise Beck, in spite of careful observation, met with no unpleasant secondary effects among his patients. He usually gave 8 to 10 tablets a day; in acute cases at the beginning of treatment sometimes up to 15 tablets. Later 6 to 8 tablets a day sufficed. The author considers the action not inferior to that of the alkaline iodides. E. Saalfeld is of opinion that iodostarin is superior to potassium iodide in many respects, as it is more slowly excreted, its action being thus protracted, and it seldom gives rise to harmful secondary effects. S. Makler also states that it is as a rule well tolerated, but cases may occur which show signs of severe iodism. When given by mouth, it appears after a short time in the urine and saliva. A part is retained in the organism and about 88 p. c. is excreted. The excretion in the urine and faeces occurs only in the form of inorganic salts of iodine. The accumulation of iodine in the body may be explained, according to Herzfeld and Makler, in that the iodine ion, set free from the organic compound, becomes attached to other organic complexes, so that the liberation of iodine is not absolutely essential.

A. Wohl carried out experiments with iodostarin in secondary and tertiary syphilis, especially in gummata, osteoperiostitis, orchitis, onychia, and in hereditary syphilis, scrofula, anaemia, etc. He also treated chronic gonorrhœal in-

Beck, Münchener medizinische Wochenschrift 1912, No. 41, p. 2232.  
\*) Compare Merck's Report 1911.

Saalfeld, Deutsche medizinische Wochenschrift 1912, No. 42, p. 1988.  
Makler, Dissertation Zürich 1912.

Herzfeld-Makler, Medizinische Klinik 1912, No. 35, p. 1428. —

Compare also J. Bakscht, Dissertation Zürich 1912.

Wohl, Pester medizinisch-chirurgische Presse 1912, No. 27.

flammation, epididymitis, hydrocele, induration and inflammation of joints with the drug. He prescribed daily doses of 6 to 8 tablets and always obtained a prompt and uniformly lasting action.

#### Iodotropon.

After a preliminary test of iodotropon, which showed that the drug was well tolerated and exercised a favourable influence on the subjective symptoms of arterio-sclerotic subjects, J. Loewy investigated the effect of iodotropon on blood pressure. He gave to patients, who apart from cardiac disturbances showed no disease of other organs, and especially no affection of the kidneys, 3 to 6 tablets of iodotropon (0.05 gramme [ $\frac{3}{4}$  grain] of iodine in each) daily for 3 weeks, and found that almost without exception the subjective symptoms were increasingly improved and there was an alteration in the blood pressure. It consisted in a fall in the blood pressure, which almost constantly affected the maximum values of blood pressure and more rarely influenced the minimum values in a majority of cases. As the uninfluenced maximum values, e. g., those found before iodotropon medication, were always above the normal limit, the author came to the following conclusion: When increased blood pressure co-existed with the clinical signs of arterio-sclerosis, the latter was always lowered by iodotropon. Further, in cases in which the pathological increase in blood pressure was not very considerable, it was markedly lowered by iodotropon. But when the blood pressure was not raised, iodotropon caused no decrease.

#### Iothion.

E. Jaeger reports upon the use of iothion\*) in dental practice. He considers the preparation to be of great service in the treatment of roots and of inflammatory processes of the periosteum, the periodontium and the gums.

For disinfecting the root canal the author employs a mixture of 25 grammes of iothion, 6 grammes of alcohol and 5 grammes of glycerin; for swabbing out abscess cavities 20 p. c. iothion; and for application to mucous membranes in exudative processes only 5 p. c. iothion. As constituents

Loewy, Deutsche medizinische Wochenschrift 1912, No. 23, p. 1091.

\*) Merck's Reports 1904—1911.

Jaeger, Deutsche zahnärztliche Wochenschrift 1912, No. 47.

for an iothion paste he recommends zinc oxide and kaolin, according to the following formula:

Rp. Zinc. oxid.	22·5 grammes (340 grains)
Kaolin.	2·5      „      ( 40    „    )
Iothion.	10·0      „      ( $\frac{1}{3}$ oz )
Glycerin q. s.	

M. Sig.: Filling paste.

According to Jaeger, this paste possesses the advantage that with provisional sealing by mastic the outer layer hardens, so that any sort of crown filling may be applied over it.

Gangrenous pulps, which have been treated for one day with the stronger iothion solution, can readily be removed, thus allowing the careful cleansing of the root canal. Before permanently sealing, the author introduces a paste consisting of 15 grammes ( $\frac{1}{2}$  oz) of zinc oxide, 5 grammes (75 grains) of kaolin and 20 grammes ( $\frac{2}{3}$  oz) of iothion. It is allowed to remain for 1 to 2 weeks and is then removed, and the filling described above is applied.

E. Herzfeld and J. B. Elin have tested various iodine preparations in the form of ointments in order to study iodine excretion and the absorption of iodine through the skin. They state that for iothion ointments vaseline forms the most suitable basis. On using a 10 p. c. iothion ointment they found a maximum excretion of 50 p. c. The use of iothion was not free from secondary effects.

### Laudanum.

The fact established by Sahli that the qualitative and quantitative action of opium, or of the total opium alkaloids, differs from the action of morphine, has led to the employment of mixtures, of which omnopon (pantopon) is probably most used at present. But, according to E. Stanton Faust, not all the alkaloids which are present in omnopon are required to effect the total opium action, as some of them may be regarded as a superfluous ballast. The author has therefore endeavoured to find mixtures of opium alkaloids, which represent the maximum opium action. In the first place, of course, morphine comes into consideration, the narcotic action of which is as a rule augmented by the

Herzfeld-Elin, Medizinische Klinik 1912, No. 9, p. 356.

Faust, Münchener medizinische Wochenschrift 1912, No. 46, p. 2490.

presence of other opium alkaloids. Its paralysing action on the respiratory centre can be mitigated or eliminated by thebaine. With regard to the so-called vomiting centre, the opposite appears to be the case, as this functional centre, which is excited by morphine, is probably reduced in functional capacity by other alkaloids. On the other hand, narcotine, narceine and papaverine do not apparently influence the tone or the emptying of the stomach of man, either by themselves or in combination with other opium alkaloids. On the ground of these pharmacologically tested facts, Faust has recommended two mixtures for therapeutic purposes, viz.:

Laudanon I, a mixture of 10 parts of morphine hydrochloride, 6 parts of narcotine hydrochloride, 1 part of codeine hydrochloride, 2 parts of papaverine hydrochloride, 0.5 part of thebaine hydrochloride and 0.5 part of narceine hydrochloride.

Laudanon II, a mixture of 10 parts of morphine hydrochloride, 2 parts of narcotine hydrochloride, 1 part of codeine hydrochloride, 0.1 part of papaverine hydrochloride, 0.5 part of thebaine hydrochloride, 0.1 part of narceine hydrochloride and 6.3 parts of milk sugar.

These mixtures represent the exact proportions in which the narcotic action of morphine is increased to the greatest extent and its action on the respiratory centre is most diminished. They should therefore be specially suitable for therapeutic purposes. Their indications are the same as those of morphine. The dosage will, on an average, be double that of morphine, thus in place of a medium dose of 0.01 gramme ( $\frac{1}{6}$  grain) of morphine, 0.02 gramme ( $\frac{1}{3}$  grain) of laudanon will be given.

### Leucofermantin.

L. Müller tried the use of leucofermantin in horses and succeeded in curing even large and extensive suppurative processes in a relatively short time with the drug\*). But, according to his investigations, leucofermantin treatment only succeeds if the area is opened up as widely as possible and open wound treatment is carried out. He therefore does

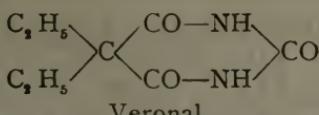
Müller, Dissertation Berlin 1912.

\*) Compare Merck's Reports 1908—1911.

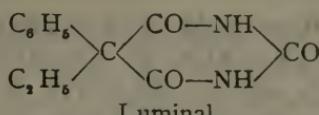
not consider the method carried out with good results in human medicine to be suitable for veterinary medicine, in which, instead of a wide incision, the abscesses are merely punctured to remove the pus and the leucofermantin is then injected into the wound cavity. He was only successful in one case, that of a small, sharply defined abscess, by the method of puncture and injection. The author bases this assertion on the grounds that, in the first place, the abscesses of horses usually contain, besides the main abscess cavity, several or even many smaller secondary abscesses, incompletely or completely separated from the main cavity and often only attaining the size of a pea; these are not opened up by the single puncture and thus remain unaffected by treatment; that, in the second place, the pus of horses is so thick in some cases that it cannot be emptied out even through a large puncture opening. The author adduces as a third reason against puncture in horses the fact that in the suppurative area there are often present dead masses of tissue which are still loosely connected with the abscess wall and cannot be removed by puncture. Added to this is the fact that in the treatment of animals the production of a good cosmetic result is not of so great importance as it is in human beings; and, besides, the scars of domestic animals, even after extensive incisions, are scarcely visible after a short time. Müller has therefore used for horses the "dry leucofermantin for veterinary use" in the form of powder and in combination with open wound treatment. He considers it very suitable for this purpose, as no dressing is required. He recommends it especially for cases in which there is danger of extension in depth, and for circumscribed suppurations, especially when the degeneration of tissue endangers neighbouring parts, such as bones and fasciae. He points out as advantages of leucofermantin the rapid cessation of purulent secretion, the avoidance of large loss of tissue, the formation of healthy granulations, and the easy and painless method of application.

#### Luminal and Luminal-Sodium.

Luminal is a body chemically related to veronal, which differs from the latter by the substitution of a phenyl group for an ethyl group.



Veronal

Diethylmalonylurea,  
Diethyl-barbituric acid.

Luminal

Phenylethylmalonylurea,  
Phenylethyl-barbituric acid.

It forms a white, crystalline powder, without odour, and with a slightly bitter taste, which melts at 173 to 174° C. It is almost insoluble in cold water, rather more soluble in boiling water. It dissolves in alkalies and in the alkaline intestinal secretion. If the alkaline aqueous solution is heated, or if it is allowed to stand for some time at the ordinary temperature, carbonic acid is evolved and a precipitate of phenylethylacetylurea is formed.

Luminal-Sodium is a white, crystalline, hygroscopic powder, readily soluble in water. It is specially suitable for subcutaneous and rectal application, while for internal use luminal will generally be preferred, which is also issued in the form of tablets (containing 0·1 and 0·3 grammes [ $1\frac{1}{2}$  and 5 grains]).

The pharmacological and clinical tests of this new hypnotic and sedative have been conducted in detail by E. Impens, Eder, W. Geissler, A. Wetzel, Graeffner, O. Juliusburger, S. Loewe, M. Goldstein, P. Schaefer, F. Sioli, W. Dockhorn, A. Hauptmann, H. König, L. Benedek, Treiber, Kino, P. Reiss, G. Emanuel,

Impens, Deutsche medizinische Wochenschrift 1912, No. 20, p. 945.  
Eder, Therapie der Gegenwart 1912, No. 6, p. 258.

Geissler, Münchener medizinische Wochenschrift 1912, No. 17, p. 922.  
Wetzel, Berliner klinische Wochenschrift 1912, No. 20, p. 937.

Graeffner, Berliner klinische Wochenschrift 1912, No. 20, p. 939.  
Juliusburger, Berliner klinische Wochenschrift 1912, No. 20, p. 940.

Loewe, Deutsche medizinische Wochenschrift 1912, No. 20, p. 947.  
Goldstein, Deutsche medizinische Wochenschrift 1912, No. 21, p. 987.

Schaefer, Berliner klinische Wochenschrift 1912, No. 22, p. 1038.  
Sioli, Münchener medizinische Wochenschrift 1912, No. 25, p. 1374.

Dockhorn, Medizinische Klinik 1912, No. 31, p. 1274.  
Hauptmann, Münchener medizinische Wochenschrift 1912, No. 35, p. 1907.

König, Berliner klinische Wochenschrift 1912, No. 40, p. 1883.  
Benedek, Wiener klinische Wochenschrift 1912, No. 42, p. 1571.

Treiber, Psychiatrisch-neurologische Wochenschrift 1912, No. 22.  
Kino, Therapie der Gegenwart 1912, No. 9, p. 403.

Reiss, Psychiatrisch-neurologische Wochenschrift 1912, No. 5, p. 49.  
Emanuel, Neurologisches Zentralblatt 1912, No. 9.

H. Meyer, M. Rosenfeld, Raecke, A. Gregor, Führer, F. Patschke, E. Szedlak, O. Geymayer, F. Moerchen and L. Romolo Sanguineti. In the opinion of these observers, the hypnotic action of luminal is equal to that of veronal and even appears to be superior to it in some respects. The more energetic action occurring in many cases is attributed to the presence of the phenyl residue in the molecule. But even without this the introduction of luminal into therapeutics is justified on the ground that in the numerous varieties and causes of insomnia a change of drug is often desirable. The pharmacological investigation of luminal has shown that the subcutaneous application of this preparation is less irritative than is that of sodium diethyl-barbiturate.

In the opinion of the authors named above, luminal is to be reckoned among the powerful hypnotics. But, according to Loewe, it has the great advantage over the hypnotics in general use that in its sedative action it approaches the efficacy of the alkaloids and exerts a greater influence on pain than do other similar drugs. In this respect it has proved specially valuable in tabes. According to Reiss, the hypnotic effect of doses of only 0·3 gramm (5 grains) is so great that it often gives rise to an astonishingly protracted action. In some cases, even after the hypnotic action had passed off, the author observed a sedative action, often lasting for 3 to 4 days. He was unable to obtain equally good results with any other drug. In agreement with this are the results of Emanuel, who finds that the sedative action of luminal takes effect in half an hour and the hypnotic action in about one hour, and is equal in strength to a scopolamine-morphine injection of 0·01 gramm ( $\frac{1}{6}$  grain) of morphine and 0·0004 gramm ( $\frac{1}{160}$  grain) of scopolamine. Schaefer also expresses

Meyer, Psychiatrisch-neurologische Wochenschrift 1912, No. 17.

Rosenfeld, Therapie der Gegenwart 1912, No. 8, p. 361.

Raecke, Medizinische Klinik 1912, No. 21, p. 865.

Gregor, Therapeutische Monatshefte 1912, No. 6, p. 413.

Führer, Münchener medizinische Wochenschrift 1912, No. 30, p. 1670.

Patschke, Neurologisches Zentralblatt 1912, p. 899.

Szedlak, Orvosi Hetilap 1912, No. 42.

Geymayer, Klinisch-therapeutische Wochenschrift 1912, No. 51, p. 1499.

Moerchen, Zeitschrift für die gesamte Neurologie und Psychiatrie 1912, No. 5, p. 517.

Sanguineti, Rassegna di studi psichiatrici 1912, Sept.-Oct.

himself well satisfied with the sedative properties of the new drug. With doses of 0·4 to 0·5 grammie ( $6-7\frac{1}{2}$  grains) he obtained prompt tranquillisation in a variety of conditions of excitement, motor restlessness and delirious mental confusion.

Eder found that, especially in tuberculous subjects, the action of luminal lasted until noon, even after small doses of 0·1 grammie ( $1\frac{1}{2}$  grains). He also found it of excellent service in apoplexy, rheumatism, gout, syphilis and heart disease.

Raecke, as a result of his experiments, considers luminal in doses of 0·2 to 0·4 grammie (3—6 grains) to be a harmless and at the same time efficacious and pleasant drug in simple insomnia. In maniacal excitement, however, it cannot replace scopolamine, as sleep sets in more slowly following its administration than after scopolamine, and this is also admitted by other authors. But luminal, in doses of 0·6 to 0·8 grammie (9—12 grains) may be depended upon with a fair degree of certainty to procure rest lasting for many hours, even in highly excited patients. With regard to the strength of action of luminal as compared with that of scopolamine, Juliusburger believes that luminal will displace scopolamine from its leading position. Only in cases in which an immediate effect is required does scopolamine, according to Loewe, come into consideration. In cases of this kind Sioli combines the two drugs, using 0·001 grammie ( $\frac{1}{64}$  grain) of scopolamine and 0·4 to 0·6 grammie (6—9 grains) of luminal for subcutaneous injection. This medication is said to be of excellent service in cases of intense excitement.

Luminal, according to Hauptmann, Kino and Geymayer, is also valuable in the treatment of epilepsy. Geymayer in particular has obtained exceedingly encouraging results. Even though luminal possesses no specific action, yet the prolonged freedom from epileptic attacks which it effects is so prompt and striking that full consideration should be accorded to the drug. This is not difficult, because the author achieved his purpose with small doses and never observed any morbid secondary symptoms or organic changes. Luminal should therefore be tried in all cases in which bromine treatment fails or has to be discontinued. The author prescribed 0·3 to 0·4 grammie (5—6 grains) for a dose when the attacks were frequent. When the excitability had improved, or when drowsiness supervened during the day, the author reduced the doses to 0·1 or 0·15 grammie ( $1\frac{1}{2}-2\frac{1}{3}$  grains), which then had

an equal effect. He states that this method of administration may be continued for weeks or months without harm.

On the whole, luminal is well tolerated, without causing any pronounced troublesome secondary effects. The fact that such a powerfully acting drug may exceptionally give rise to secondary effects, such as lassitude, headache or rash in sensitive subjects, should not interfere with its general employment. Moreover, occurrences of this kind can readily be avoided by commencing with small doses of 0·2 grammie (3 grains) and only passing on to larger doses when the patient's tolerance for luminal has been tested. It may be noted that luminal does not give rise to cumulative action.

To sum up, the following are the indications for luminal as a hypnotic and a sedative: All forms of agrypnia, including those accompanied by physical pain, as for example rheumatism, gout and syphilis; further, psychiatric cases, such as conditions of moderate and intense excitement, delirium, state of depression, cure of the morphine habit, epilepsy, etc., katatonia and general paralysis. In the insomnia and restlessness of old age, in arterio-sclerosis, etc., luminal is often of service, but it must be remembered that it is an energetic drug.

The following remarks apply to the dosage of luminal:

**I n t e r n a l a d m i n i s t r a t i o n .** In uncomplicated, nervous agrypnia 0·2 to 0·3 grammie (3—5 grains) of luminal will usually suffice. In conditions of excitement of moderate degree, the average dose is 0·3 to 0·4 grammie (5–6 grains). Only in severe motor restlessness are doses of 0·6 to 0·8 grammie (9—12 grains) required. 0·8 grammie (12 grains) may be considered the maximum dose. Smaller doses should be given to women and to weakly men. For phthisical patients doses of 0·1 grammie ( $1\frac{1}{2}$  grains) often suffice. After 4 to 5 days it is well to allow two days' interval in the administration of luminal.

**S u b c u t a n e o u s a d m i n i s t r a t i o n .** For this purpose a 20 p. c. solution of luminal-sodium is used, which is prepared by dissolving the luminal-sodium in boiled water which has cooled to 30° C. 2 c. c. of this solution correspond to 0·4 grammie of luminal-sodium. The subcutaneous dose is somewhat larger than the internal dose because luminal-sodium corresponds to only 90 p. c. of luminal; to women 0·4 to 0·5 grammie (6—7 $\frac{1}{2}$  grains), to men 0·5 to 0·6

gramme ( $7\frac{1}{2}$ —9 grains) are given. In chronic cases and old people a dose of 0·3 to 0·4 gramme (5—6 grains) is often sufficient. The hypnotic effect sets in rather later after subcutaneous application of luminal than following internal administration. According to the instructions of various authors (König, Moerchen), subcutaneous injections should be made, not into the skin, but deep into the subcutaneous tissue and into the loosest possible layers of it.

**Rectal administration.** 0·4 to 0·5 gramme (6 to  $7\frac{1}{2}$  grains) of the readily soluble luminal-sodium are administered in aqueous solution as enemata, or in the form of suppositories.

#### **Magnesium-Perhydrol.**

The irrigation and emptying of the stomach customarily carried out in cases of chronic insufficiency of the motor activity of the stomach not only inconvenience the patients, but may in time lead to threatening symptoms of collapse on account of over-exertion or of too great abstraction of chlorides from the weakened organism. But, according to M. Gockel, both the irrigation and the expression may be reduced or entirely avoided if, besides a regulated diet and any symptomatic measures which may be required, such as rectal saline infusions, nutrient enemata, etc., energetic antacid and anti-fermentative treatment is carried out. In the author's experience, the administration of magnesium-perhydrol serves this purpose; it has a favourable effect not only on the superficial congestive process, but also on the symptoms accompanying and following it.

The action of the preparation is not difficult to explain if it is borne in mind that it is decomposed in the stomach by the action of the acid secretion into hydrogen peroxide, or oxygen and magnesium oxide, or the magnesium salts of the acids which are present. The hydrogen peroxide thus formed deodorises and oxidises the foul smelling, stagnating ingesta and the putrefactive products arising as a result of the congestion, and thus the possibility of auto-intoxication is diminished. The neutralisation of the acids by the mag-

nesium oxide acts as an antizymotic, as the chief fermentative organisms present, e. g., yeast and lactic acid bacilli, grow badly in weakly acid or alkaline fluids and are soon destroyed. Thus the magnesium oxide assists the oxidising, deodorising and antifermentative action of the perhydrol. One consequence of the alteration of the gastric contents by the products of decomposition of magnesium-perhydrol is that traumatic inflammatory irritation of the mucous membrane is prevented or at any rate weakened. Consequently the reflex spasm of the musculature does not take place or only takes place to a slight degree, and thus the organ is spared and the emptying of the ingesta into the intestine is hastened.

In the intestine the magnesium oxide or the magnesium salts cause increased peristalsis and lead to the painless removal of constipation, which is usually present in chronic motor insufficiency, and thus relieve the patient in this direction also.

Gockel attributes the improvement in the morbid condition of his patients to the substances named above, which are formed in the stomach from magnesium-perhydrol. He reports that after a few days the gastric spasm had entirely or for the most part disappeared, the diuresis increased and the feeling of thirst and fullness were cured or greatly relieved. The medication had an equally good effect upon eructations, vomiting, increase of appetite and evacuation of the bowels. In simple stenosis, as in carcinoma, the weight increased during the first weeks of treatment.

In one case of extensive squamous celled carcinoma with metastases in the liver, and in one case of carcinomatous and cicatricial pyloric stenosis with absolute insufficiency, magnesium-perhydrol failed, as did the gastric irrigation carried out for the sake of comparison.

Magnesium-perhydrol is, according to the author's instructions, given 3 to 4 times a day in doses of one tea-spoonful on an empty stomach. If the motions are too frequent, the bowels are regulated by the administration of 15 drops of a 1 p. c. morphine solution 1 to 3 times a day.

For the treatment of acidosis in diabetes mellitus, von Noorden reports that besides the fixed alkalies magnesium-perhydrol is specially suitable. It is far superior to the usual preparations of magnesia, which might be considered

on account of the tendency to constipation; it may also be recommended for prolonged use. It is also indicated, according to L. Carozzi, for the digestive troubles of persons who come much into contact with lead (lead workers and compositors). It is said to be of great use in these cases.

Mention may be made of an observation of R. von Engelhardt, which possibly points to a new use for magnesium-perhydrol. A lady patient of the author's had an idiosyncrasy to fruit acids, vinegar and certain vegetables and these substances always gave rise to exanthemata and hyperæmia of the pharyngeal mucous membrane. But if she took magnesium-perhydrol she could digest any mixed diet excellently.

### Magnesium Sulphate.

Further communications on the value of magnesium sulphate in tetanus\*) have been furnished in the past year by J. Camus, O. Smithson, G. Parker, E. Pallasse and Th. Kocher. According to these reports, the value of intradural injections of magnesium sulphate has not yet been unanimously established. At any rate the opinions vary greatly.

Camus carried out experiments on dogs with magnesium sulphate, carbolic acid and tetanus antitoxin, which resulted in favour of the antitoxin. The author considers that magnesium sulphate and carbolic acid did not influence the morbid process. In his opinion the magnesium salt only reduces the irritability for a very short time. One of his animals, which he had treated simultaneously with magnesium sulphate and carbolic acid, did not outlive the control animals. This failure is probably due to the fact that neither the magnesium salt nor the carbolic acid affect the tetanus toxin. For this reason the antitoxin, which fulfils this condition to some

Carozzi, Pensiero medico 1912, 25<sup>th</sup> February.

Engelhardt, Petersburger medizinische Wochenschrift 1912, No. 12, p. 190.

\*) Compare Merck's Reports 1906—1911.

Camus, Paris médical 1912, p. 527. — Therapeutische Monatshefte 1912, p. 203 and 678.

Smithson, British Medical Journal 1912, I, p. 181.

Parker, Journal of the American Medical Association 1912, Vol. 58, 8<sup>th</sup> June, No. 23.

Pallasse, Provence médicale 1912, No. 34.

Kocher, Korrespondenzblatt für Schweizer Ärzte 1912, No. 26.

extent, proved much more efficacious. Smithson considers magnesium sulphate to be an efficacious drug, the correct dosage of which is not yet sufficiently well known. In a case of tetanus, injections of 1 c. c. of a 25 p. c. magnesium sulphate solution effected the disappearance of the spasmodic attacks, but they could not prevent the fatal issue.

Parker reports three cases which were cured by magnesium sulphate treatment. In these cases the antitoxin treatment had failed. It is noteworthy that the author exceeded the dose of 1 c. c. of the 25 p. c. solution to 10 kilogr. of body-weight without observing troublesome secondary effects. Very good results were also obtained by Kocher, who cured 3 cases by means of intradural injections of magnesium sulphate. He gave several injections of 2 to 5 c. c. of a 25 p. c. solution, which always suppressed the spasms for several hours.

Several of the authors draw attention to the fact that the injections of magnesium sulphate may, under certain conditions, be attended by danger. Depression of the respiratory centre, lowering of the blood pressure and secretion from the bronchial mucous membranes have been observed. In one of Kocher's cases 3 injections of 5 c. c. of the 25 p. c. solution given within 2 days were followed by very deep narcosis with cessation of respiration, which was relieved by tracheotomy and inhalations of oxygen. He therefore recommends the use of a 15 p. c. solution, as this is even of more value than chloral hydrate. He advises that the treatment be combined with injections of tetanus antitoxin. Doses of 10 c. c. of the 15 p. c. solution of magnesium sulphate may be injected on several consecutive days. The distribution of the magnesium sulphate in the lumbar sac is to be regulated by placing the patient in a suitable position. Parker, who has only observed bronchorrhœa as a troublesome symptom following treatment by injection of magnesium sulphate, suggests that physostigmine should be administered to counteract this effect.

W. F. Boos, G. Ocana, Bouchut and Devic also dwell upon the toxic action of magnesium sulphate. It is certainly an individual action and is very probably due to

the high concentration of the solutions, for concentrated solutions of sodium sulphate may give rise to similar symptoms. In rabbits the intraperitoneal injection of 1.5 grammes of magnesium salt per kilogramme of body-weight is required to kill the animal. The internal administration of 15 grammes of magnesium sulphate in 20 c. c. of water proved fatal.

According to Rocaz, injections of magnesium sulphate into the lumbar canal have also proved useful in chorea. He first withdrew 10 c. c. of cerebro-spinal fluid and then injected 2 c. c. of the 25 p. c. solution. The patient was placed in such a position that the injection fluid was able to reach the upper part of the spinal canal. A few hours after the injection the choreic movements ceased in the lower extremities and later in the upper extremities also. Twitchings of the face are more obstinate in character and a second injection may be necessary to get rid of them. But the treatment requires caution, especially among children, as it is not altogether free from danger.

The anæsthetising action of magnesium sulphate, which has also been described by B. Wiki in experiments on animals, led A. B. Jackson to carry out experiments in acute articular rheumatism and angina. In severe cases of acute articular rheumatism it is necessary to give intramuscular injections of 4 c. c. of the 25 p. c. solution daily for 4 to 5 days and at the same time to treat the inflamed joints with compresses soaked in a saturated aqueous solution of magnesium sulphate. For angina similar compresses are applied to the neck.

As special interest has recently been directed to the subcutaneous administration of drugs for stimulating peristalsis, attention may be drawn to the communications on the subcutaneous administration of magnesium sulphate as a purgative, which has been discussed by Robin, Sourdèl and Carnot. Robin and Sourdèl recommend the subcutaneous injec-

Rocaz, Klinisch-therapeutische Wochenschrift 1912, No. 7, p. 227.  
Wiki, Archives internationales de pharmacodynamie 1911, Vol. 21,  
p. 415.

Jackson, Practitioner 1912, Vol. 88, p. 177.

Robin-Sourdèl, Bulletin de la société médicale des hôpitaux de Paris 1912, p. 881. — Klinisch-therapeutische Wochenschrift 1912, No. 37, p. 1095. — Presse médicale 1912, No. 50, p. 529.

Carnot, Paris médical 1912, p. 102. — Therapeutische Monatshefte 1912, No. 11, p. 819.

tion of 1 c. c. of the 25 p. c. solution, preferably made in the abdominal region, if for any reason the internal or rectal employment is to be avoided. It is said that very satisfactory results are obtained by means of this treatment. The stools, according to the observations of the two authors, are almost always formed and only seldom fluid. If the injection is not successful, it may be repeated. There is, as a rule, no advantage in giving larger doses, as they are often less efficacious than the suggested dose. Sourdel has even found that in cases in which 0·25 grammes of magnesium sulphate had failed, half the dose effected the desired result. The authors attribute the action of the injections to the increase of peristalsis, but Carnot does not believe this to be the case. Nor did he find the action of the injections to be constant. As concentrated solutions of magnesium sulphate cause irritation, he uses a 1 p. c. solution, of which he injects 2 to 20 c. c. The subcutaneous application is said to have the advantage over the internal administration in that its action is milder and more lasting.

### Maltyl.

This nutritive and strengthening preparation\*) has been prescribed for children by E. Villain. He gave it to weakly children, in whom it was desired to supplement a natural invigorating diet by an artificial strengthening remedy, with the result that the appearance and the appetite of the children were improved, and in many cases they increased in weight. In irregularity of the heart in anaemic children and after diphtheria, he used triferrin-maltyl, the prolonged use of which regulated the cardiac action. Older children are given a teaspoonful of triferrin-maltyl 3 times a day; for younger children a teaspoonful of maltyl is added to each bottle.

To meet the requirements of sportsmen, for whom, besides a nutrient and strengthening preparation, a stimulant is also needed, maltyl has recently been combined with maté (Paraguay tea) in the form of tablets. A tablet weighing 5 grammes (75 grains) contains 0·02 grammes ( $\frac{1}{3}$  grain) of caffeine, and a little cocoa to improve the taste. These maltyl-maté tablets

\*) Compare Merck's Report 1911.

Villain, Deutsche Medizinal-Zeitung 1912, No. 17.

Nippe, Medizinische Klinik 1912, No. 38.

may be used as a stimulant in sports, and also for people who are easily exhausted. Nippe tested the preparation during a six days' race among some athletes. His results justify the further testing and employment of the preparation. As the small amount of caffeine contained allows 75 tablets to be taken with safety, maltyl-maté, according to Nippe, indeed appears to be a desirable stimulant and strengthening preparation for athletes. The use of such large doses is, of course, only intended for special performances; they cannot be repeated daily or at any rate not for more than a few days. Small amounts, about 20 tablets, are entirely harmless.

### Mastic.

Mastisol\*), recommended by von Oettingen for wound dressings, is, according to W. Spindler, a modification of the skin varnish introduced in 1900 by the orthopædic surgeon Fink of Kharkoff, and known as "Fink's skin varnish" or "Cleol". Its formula is:

Rp. Terebinth. venet.	15.0	grammes	( $\frac{1}{2}$ oz)
Mastic	12.0	„	(180 grains)
Resin.	25.0	„	( $\frac{5}{6}$ oz)
Resin. alb.	8.0	„	(120 grains)
Alcohol (90 p. c.)	180.0	„	(7 oz)
Misce et filtra.			

The method of employment is as follows: In wounds of the hairy scalp, the surrounding area is carefully shaved or the hair is merely cut short, care being taken not to touch the edges of the wound. The wound is not to be touched either with the fingers or with a plug of cotton wool, etc. Nor is irrigation permissible with any sort of fluid. Gross dirt is removed mechanically from the wound by means of sterile forceps and the surrounding area is swabbed with alcohol or with tincture of iodine. Then the edges of the wound are approximated and the skin varnish is applied by means of a brush or a plug of cotton wool to the wound and the surrounding area, over a sufficient extent to allow the dressing to be firmly fixed. After waiting until the application has become sticky, the Marly bandage is firmly wound round. The dressing is left in place until healing

\*) Compare Merck's Report 1911, p. 304.

Spindler, Petersburger medizinische Wochenschrift 1912, No. 2, p. 24.

has resulted, unless suppuration occurs. This method has proved highly successful in more than 2000 injuries and operation wounds, among which were a number of torn and crushed wounds in factory workers. Although most of the wounds were not in a particularly favourable condition for healing, yet the results were excellent. Only 6 p. c. of the cases suppurated. Clean wounds, such as cuts, which were treated immediately, and operations wounds healed by first intention in 100 p. c. of the cases.

Krebser used a solution of 20 grammes ( $\frac{2}{3}$  oz) of mastic and 1 gramme (17 min.) of linseed oil in 50 grammes ( $1\frac{1}{6}$  oz) of chloroform for the treatment of operation wounds, and cellulose-wool sewn up in muslin for dressings. The author rejects as unfounded all the objections which have been raised against mastic dressings, and besides pointing out the favourable healing results, he claims the following advantages for the method: 1. Avoidance of all cleansing processes which are injurious to the wound and cause pain; 2. Independence of water; 3. Great simplicity of the process, which can easily be learned by laymen; 4. Great saving of time; 5. It can be used in those parts of the body to which it is difficult to apply bandages; 6. The dressing cannot be displaced; 7. Cheapness; 8. It does not irritate the skin, and 9. Security against infection.

A. Suter obtained the same favourable results with mastisol in the treatment of operation wounds. He states that the preparation irritates the skin less than is the case with Grossich's method of disinfection by iodine. Further, the asepsis effected by the mastic dressing lasts for a very long time. The dressing can readily be removed by means of benzine. A. Wagner also expresses a very favourable opinion on the treatment of wounds by mastisol.

O. Neugebauer found mastisol very useful in burns and corrosions of the second and third degree. He painted the entire affected area with mastisol and covered it over with cotton wool. If the wound discharged serum he applied fresh gauze, but he only renewed the entire dressing if severe

Krebser, Beiträge zur klinischen Chirurgie 1912, Vol. 79, p. 129.

Suter, Korrespondenzblatt für Schweizer Ärzte 1912, p. 823.

Wagner, Zentralblatt für Chirurgie 1912, No. 35, p. 1190.

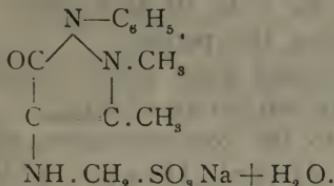
Neugebauer, Wiener klinische Wochenschrift 1911, p. 379.

complications occurred. In a few cases certainly these were so great that the dressing had to be discarded.

Von Oettingen has recently combined mastisol with other wound dressings and he recommends 2 p. c. chrysarobin-mastisol, 20 p. c. naphthalan-mastisol, and 2 p. c. iodine-mastisol.

### Melubrin.

Melubrin is the sodium salt of phenyl-dimethyl-pyrazolonamidomethane-sulphonic acid, of the chemical formula:



It forms a white, crystalline powder, soluble 1 in 1 of water, soluble in methyl alcohol in the proportion of 1:10; it dissolves with difficulty in alcohol and is practically insoluble in the other ordinary organic solvents. At 231—233° C. it begins to melt with decomposition.

Melubrin, which is chemically related to antipyrine, was carefully studied clinically by Loening. According to the author's results, it is an antipyretic which is efficacious in doses of 0.5 to 1 gramme ( $7\frac{1}{2}$ —15 grains) and which is even tolerated without the occurrence of any secondary symptoms in daily doses of 8 grammes (120 grains) — 2 grammes (30 grains) 4 times a day. But for children and in ambulatory treatment, until the action of melubrin has been more closely investigated, the author considers that daily doses of 5 grammes (75 grains) should not be exceeded.

The action of the drug should be carefully watched in debilitated patients before proceeding to the use of large doses. The author never observed the occurrence of toxic symptoms, such as occur with antipyrine.

Melubrin is especially indicated in acute articular rheumatism. It acts as a specific in these cases, like salicylic acid, if it is administered 3 to 4 times a day in doses of 1 to 2 grammes (15—30 grains). No action on the heart was observed, nor was the pulse rate increased. The drug can

also be given in endocarditis. Melubrin medication did not give rise to unpleasant outbreaks of perspiration; these were always considerably milder than would have been the case had salicylic acid been given. A relapse occurred in isolated cases of acute articular rheumatism, but according to the author's observations, this is more rarely the case than when sodium salicylate is used. As soon as the desired effect has been attained, in severe articular rheumatism the administration of melubrin is continued with small doses (1 gramm [15 grains] 3 times a day) for 8 to 10 days longer and the patients are kept in bed during this period.

Loening obtained good results in chronic articular rheumatism, myositis and severe sciatica.

According to the communications of other authors, such as Krabbel, Riedel, Hoppe, J. Müller, Engelen, Staffeld, Th. Schrenk, P. Neukirch, H. Treber, A. Lewandowski and Saar, Loening's statements have for the most part been confirmed in practice. The analgesic action of the drug was especially manifest in acute, subacute and chronic rheumatic polyarthritis, in muscular rheumatism, sciatica, influenza and in the lightning pains of tabes; the antipyretic action especially in pneumonia, broncho-pneumonia, bronchitis, febrile phthisis, pleurisy and pericarditis, and in endocarditis and scarlet fever. Treber also obtained a good result in a case of gout, but in another case the preparation failed. Hoppe's experiments in gout did not give a positive result. The use of large doses appears to be essential for success in rheumatism; they can, if necessary, be given successfully by rectum, as Staffeld reports. He gave 3 grammes (45 grains) a day in one case. Large doses may usually be given without apprehension, because, according to the above named authors, secondary symptoms rarely occur. But they are not always

Krabbel, Medizinische Klinik 1912, No. 16, p. 654.

Riedel, Therapie der Gegenwart 1912, No. 5, p. 208.

Hoppe, Berliner klinische Wochenschrift 1912, No. 22, p. 1040.

Müller, Wiener klinische Wochenschrift 1912, No. 25, p. 960.

Engelen, Therapie der Gegenwart 1912, No. 8, p. 360.

Staffeld, Münchener medizinische Wochenschrift 1912, No. 33, p. 1810.

Schrenk, Deutsche medizinische Wochenschrift 1912, No. 34, p. 1588.

Neukirch, Therapeutische Monatshefte 1912, No. 9, p. 645.

Treber, Medizinische Klinik 1912, No. 45, p. 1833.

Lewandowski, Therapie der Gegenwart 1912, No. 12, p. 574.

Saar, Deutsche medizinische Wochenschrift 1912, No. 52, p. 2455.

absent. Rashes, vomiting and gastric trouble have been observed. It may be noted that after the employment of melubrin, a reducing substance is occasionally found in the urine; according to Borutta's investigations it consists of glycuronic acid.

Large doses are not suitable for the treatment of the fever of phthisical subjects; experience shows that single doses of 0·25 to 0·5 gramme ( $4\frac{1}{2}$  grains) usually suffice. Schrenk first gave 0·5 gramme ( $7\frac{1}{2}$  grains) 3 times a day in tuberculosis, and if this did not suffice, he increased it after a few days to 3 single doses of 1 gramme (15 grains). He found that a certain degree of summation frequently occurs. If melubrin only causes an insignificant depression of temperature on the first day, the same dose may have a much more marked effect on the second day. Hoppe has met with such severe outbreaks of perspiration and shivering after doses of 1 gramme (15 grains) (3 gramme [45 grains] a day) that the patient refused further treatment. He obtained satisfactory results, however, with small doses. He therefore administered a teaspoonful or a tablespoonful of an aqueous solution of melubrin 5 to 6:200 seven times a day.

According to Riedel, arthritic troubles are cured more quickly by a combination of melubrin (1 gramme [15 grains]) and acetyl-salicylic acid (0·5 gramme [ $7\frac{1}{2}$  grains]) than by melubrin alone. But whereas Riedel, among others, found that the administration of melubrin caused the simultaneous disappearance of articular pain and swelling, Treber was under the impression that the articular swellings did not disappear so rapidly as when sodium salicylate and acetyl-salicylic acid were employed. Very rarely did the antipyretic action fail, more frequently the analgesic action, and comparatively most frequently the articular swellings remained uninfluenced or were only partially influenced by melubrin. A few of these last-named cases were cured in a short time by the use of salicylate preparations, but the majority were only cured by the prolonged use of this drug, with the simultaneous employment of diaphoretics.

### Menthol.

Headaches are very frequently caused by chronic hypertrophic processes of the nasal mucous membrane, by dryness of the nose and by stagnation and retention of the nasal secretion, or by blocking of the nares generally. Therefore,

according to A. Lorand, headaches should be treated by way of the nose. This is most readily effected by means of a snuff having the following composition:

Rp. Menthol. 0·5 grammie ( $7\frac{1}{2}$  grains)

Acid. boric. 1·0 grammie (15 „ )

Rhiz. Iridis flor.

Sacch. lactis aa 2·0 grammes (30 „ )

or:

Rp. Herb. Majoran.

Rhiz. Iridis flor. aa 1·0 grammie (15 grains)

Sacch. lactis 2·0 grammes (30 „ )

Rhiz. Veratr. alb. 0·14 grammie (2 „ )

M. Ft. pulv. non subtilissimus.

The latter mixture is said to have the stronger action. If it is not efficacious, 0·04 grammie ( $\frac{2}{3}$  grain) of veratrine may be added to every 5 grammes (75 grains) of powder, but it must be remembered that the mixture is then no longer harmless and the single doses must not be too high. Snuffs have the advantage over internal medication that they cannot have an injurious effect upon the internal organs, notwithstanding which they act with comparative rapidity.

In the treatment of acute coryza, menthol has also found much favour on account of its action in reducing congestion. A. Heindl has recently reported upon this employment of menthol and its effect. He, like many before him, has no doubt of the great utility of menthol in coryza and in certain diseases of the upper air passages, but recently secondary effects have been observed in children, so that the preparation should only be used for children with a due amount of care and in suitable doses. According to R. Leraux, excessive use of menthol in the nose should be avoided, as it may give rise to inflammation of the mucous membrane, hypersecretion, irritation of the pharynx, erythema of the face, nose and mouth, etc. The author entirely disapproves of the use of menthol for children, especially for young babies. In order to avoid the secondary effects of menthol in adults,

Lorand, Münchener medizinische Wochenschrift 1912, No. 41, p. 2226.  
Heindl, Ärztliche Reformzeitung 1912, No. 8, p. 95.

Leraux, Annales des maladies de l'oreille, du larynx, du nez et du pharynx 1911, Vol. 37, No. 9. — Répertoire de pharmacie 1912, p. 162.

W. Lublinski considers that the administration of menthol mixtures of unknown composition should be avoided. Instead of the large doses suggested in the literature, he does not prescribe more than 0·2 to 0·5 grammes ( $3-7\frac{1}{2}$  grains) of menthol to 100 grammes (4 oz) of liquid paraffin, 10 to 15 drops of which he instils into each nostril by means of a pipette. The patient bends his head back as far as possible and after the instillation of the solution he plugs the nose for a few minutes with a small tampon of cotton wool. Gentle massage is applied and the medicament is distributed in the nose and in the posterior pharyngeal wall. Lublinski excludes children under eight from treatment by menthol, because he observed an untoward secondary effect in a child aged 11 months, even on using a mild preparation of menthol in only 2 p. c. solution\*).

For the alleviation of the intolerable itching occurring in obstruction of the bile-duct, R. Kolisch suggests besides hot water and bran baths, the application of the following ointment to the affected parts:

Rp. Menthol.

Chloral hydrat.

Camphor. aa 10·0 grammes ( $\frac{1}{3}$  oz)

Vaseline 70·0 „ ( $2\frac{1}{3}$  oz)

Sabatié also uses a menthol solution to relieve itching (in urticaria). It is used in the form of a spray and consists of 10 grammes ( $\frac{1}{3}$  oz) of menthol, 30 grammes (1 oz) of spirit of camphor, 30 grammes ( $\frac{2}{3}$  oz) of chloroform and 30 grammes ( $1\frac{1}{3}$  oz) of ether.

The therapeutic value of the radioactive iodine-menthol, so-called "dioradin"\*\*), in pulmonary tuberculosis is discussed by W. St. Wells, C. Wall, G. Dromard, S. K. Andronow

Lublinski, Berliner klinische Wochenschrift 1912, No. 6, p. 261.

\*) Compare the article on Coryfin.

Kolisch, Wiener medizinische Wochenschrift 1912, p. 654.

Sabatié, New York Medical Journal 1912, p. 1275.

\*\*) Compare Merck's Report 1911, p. 313.

Wells, Revue internationale de la tuberculose 1912, Vol. 22, p. 170.

— Allgemeine medizinische Zentralzeitung 1912, No. 41, p. 537 and No. 42, p. 551.

Wall, British Medical Journal 1912, II, p. 109.

Dromard, Zentralblatt für die gesamte Therapie 1912, No. 10, p. 505.

Andronow, Revue internationale de la tuberculose 1912, Vol. 22, p. 201.

and R. A. Stoney. According to Wells, the action of dioradin treatment consists in the improvement of the appetite and of digestion, the decrease in the cough and expectoration, the fall of the temperature, strengthening of the pulse, increase in weight and diminution of tubercle bacilli. The treatment is simple and safe. Renal lesions alone constitute a contraindication. Wells' results are for the most part confirmed by the other authors; Wall alone was not convinced of the special efficacy of dioradin. According to M. Berliner, menthol and iodine without radium are just as effective as dioradin. He uses the following mixture for the treatment of tuberculosis:

Rp. Menthol.	10·0	grammes (1/3 oz)
Eucalyptol.	20·0	„ (2/3 oz)
Iodipin. (25 p. c.)	50·0	„ (1 2/3 oz)

At the commencement of treatment he injected 1 c. c. (17 min.) a day subcutaneously and later the same dose at intervals of 1 to 2 days. He never observed the slightest sign of disturbance, whereas with dioradin the possibility of iodine poisoning is admitted. The mixture given above acts beneficially, like dioradin, on cough, sleep and temperature, and, if suitably prepared and applied, it does not give rise to the slightest trouble.

### Mercuric Cyanide.

For puerperal infections Souligoux employs intramuscular injections of mercuric cyanide. Without curetting or other local measures he injects a solution of 0·01 gramme of mercuric cyanide and 0·01 gramme of stovaine in 1 c. c. of water daily for a week. If toxic symptoms occur, the injections are discontinued; if the result is not satisfactory, the injections are repeated. As he obtained an immediate improvement of the general health in a large number of cases by this method, he considers its clinical value to be established.

Mariotti employs mercuric cyanide for the abortive cure of syphilis in the first stage of the disease. Besides

Stoney, Klinisch-therapeutische Wochenschrift 1912, No. 9, p. 287.  
Berliner, Berliner tierärztliche Wochenschrift 1912, No. 9, p. 408.  
Souligoux, Bulletins et mémoires de la société de chirurgie de Paris 1912, Vol. 38, p. 368.

Mariotti, Giornale italiano delle malattie veneree e della pelle 1912, Vol. 52, p. 229.

rendering the primary affections and the enlarged inguinal glands hyperæmic by means of Klapp's suction apparatus, he injects 1 c. c. of a 0·5 p. c. solution of mercuric cyanide into the inguinal region every day. Six injections are given a week, and 30 to 50 injections in all. Besides this, 1 c. c. of a 0·25 p. c. solution is injected subcutaneously in the neighbourhood of the sclerosis and into the skin of the penis daily, the area of injection being lightly massaged and 30 p. c. calomel ointment applied. 12 to 14 injections of the 0·25 p. c. solution usually suffice, but a larger number may be given. By means of this treatment Mariotti claims to have suppressed the secondary symptoms, and to have prevented Wassermann's reaction becoming positive.

Fernet and Ettinger combined the injection of mercury with salvarsan, for experience has shown that mercurial treatment is assisted by arsenic. By the simultaneous use of mercuric cyanide, smaller doses of salvarsan suffice and the dangers caused by too large doses of the latter are avoided. In recent cases without secondary symptoms and with a negative Wassermann reaction, the authors injected 0·3 to 0·4 grammes of salvarsan twice within a week. This treatment was supplemented by a series of mercuric cyanide injections, consisting of 10 to 12 intravenous injections of 0·01 to 0·015 grammes of mercuric cyanide given at intervals of 2 days. In the presence of secondary symptoms 12 to 15 injections were given. The secondary effects of salvarsan and mercuric cyanide were insignificant, while the result of the combined treatment was very encouraging. To prevent recurrences, the authors recommended injections of yellow mercurous iodide at the conclusion of treatment, even when the Wassermann test yields a negative result.

### Mercurous Nitrate.

According to E. Kafka, mercurous nitrate in combination with potassium iodide constitutes a very sensitive test for tungstates and molybdates. To carry out the test, a drop of a saturated solution of mercurous nitrate is added to the neutral solution which is to be tested for tungstates or

Fernet-Ettinger, *Progrès médical* 1911, No. 41. — Wiener klinische Wochenschrift 1912, No. 10, p. 392.  
Kafka, *Zeitschrift für analytische Chemie* 1912, No. 7, p. 483.

molybdates, and after the addition of 1 to 1.5 c. c. of concentrated hydrochloric acid, an excess of potassium iodide is added. On shaking, the green precipitate first formed is redissolved, and in the presence of tungsten or molybdenum a blue solution results. Concentrated solutions of a tungstate, besides separation of mercury, give a blue precipitate soluble in hydrochloric acid. The reaction is so sensitive that 0.2 mg. of sodium tungstate can be detected. If iodine is gradually separated from the mixture by prolonged standing or by heating, the blue substance is oxidised and the solution is coloured yellow. To test for molybdenum, potassium sulphocyanide is added to the blue solution, whereupon the blue molybdenum compound immediately turns blood-red. If the amount of molybdenum present is so small that no blue coloration results, the addition of potassium sulphocyanide causes the formation of an orange-yellow substance which is dissolved by ether on shaking the liquid with it.

### Merjodin.

Merjodin\*), according to A. Erdös, is a very reliable preparation of mercury in the treatment of secondary and tertiary syphilis; its administration by mouth is simple and convenient. The drug is well tolerated by the stomach and intestine. It does not interfere with the digestion and on account of its mild aperient action even appears to have a beneficial influence on the functions of the digestive organs.

Even though merjodin is frequently useful by itself, yet in metasyphilitic symptoms, in nerve syphilis and in those cases in which a very energetic course of mercury is required, the combination of the drug with other measures and preparations may be recommended. In the early stage, however, and in chronic, intermittent treatment, merjodin is just as useful as mercury injections or inunctions. As it is less troublesome than inunctions, the patient does not so easily neglect the medication on account of inconvenience or of lack of time. Erdös recommends as a first dose one tablet (0.0025 gramme [ $\frac{1}{25}$  grain] of mercury) 3 times a day, which is to be well chewed before swallowing. In severe cases 4 to 5 tablets a day may be given as an initial dose. If the

\*) Compare Merck's Report 1911.

Erdös, Deutsche medizinische Wochenschrift 1912, No. 18, p. 856.

patient takes the medication well, the dose may be increased in moderately severe cases to 3 tablets 3 times a day, best taken after meals. Should intestinal irritation and diarrhoea occur, the drug is left off for a few days. This treatment must, of course, be accompanied by scrupulous attention to the mouth.

### Mescaline Sulphate.

As I reported years ago\*), mescaline, one of the alkaloids of Anhalonium Lewinii, according to Heffter, possesses the property of causing intoxication accompanied by brilliant colour visions. But the author at the same time pointed out that the alkaloid occasions such unpleasant by-effects that the enjoyment of the beautiful visions is much diminished, and there need be no apprehension that the alkaloid will be introduced among civilised nations as a means of intoxication. Bresler later carried out experiments on mentally affected patients, in order to make a more detailed study of the therapeutic value of mescaline. He came to the conclusion that no other pharmacological drug, without giving rise to disturbances of consciousness and marked by-effects, exerted such a powerfully excitant action on a circumscribed area of the cerebral cortex as did mescaline. His observations of the definite excitation of the senses led him to the assumption that this reaction affected the excitability of the optical cortex cerebri, which is distinct from the retinal impressions. The results of the investigations of the above named authors did not lead to practical conclusions for psychiatry. For this reason a new work by A. Waeber is not without interest. In order to investigate in greater detail the curious intoxicating effect produced by mescaline, he administered subcutaneous injections of 0.2 gramm (3 grains) of mescaline sulphate to several persons and followed up the subjective and objective effects. But among 6 persons he did not once meet with the visions described by Heffter and Bresler. Only one person was affected by drowsiness and during sleep saw a coloured picture and heard strange music. But, according to Waeber, in-

\* ) Compare Merck's Reports 1896, p. 166; 1898, p. 34, 156.  
Heffter, Archiv für experimentelle Pathologie 1894, Vol. 34, p. 65;  
1898, Vol. 40, p. 385.  
Bresler, Psychiatrisch-neurologische Wochenschrift 1905, No. 27.  
Waeber, Petersburger medizinische Wochenschrift 1912, No. 2, p. 17.

dividual importance can only be attached to this fantastic dream inasmuch as the particular person rarely dreams naturally. The facial symptoms, which occurred in all the individuals, were in all probability chiefly caused by peripheral irritation. This may be inferred from the observed contrast colours, the dilated pupils, twitching of the eyes, etc. In three experiments there were well marked hypnagogic conditions, during which imaginary movements and faces were seen. Usually the mood became cheerful, there was a tendency to laugh and motor restlessness, the patient was easily diverted, the memory and the ability to calculate were reduced, there was a tendency to unite words by their sound and a more or less rapid cessation of the representations. Among the physical symptoms were sensations of smell, a feeling of weight in the head, slackness, lassitude, a feeling of heat in the joints, vomiting, a feeling of protrusion of the eye-balls, vasomotor appearances, outbreaks of perspiration and increased lacrymation. The double personality observed by Dixon was not definitely present. These results did not confirm Bresler's findings. Nor has the hope been fulfilled that by means of researches on mescaline, the sensation of double personality, said to be brought about by mescaline and which is often described by mentally affected patients, might be explained.

### Mesothorium and Thorium X.

Mesothorium, discovered in 1907 by Hahn, is the first radio-active decomposition product of thorium. Theoretically it consists of mesothorium I, the half value period\*) of which is 5.5 years, and of mesothorium II, the half value period of which is 6.2 hours. The  $\beta$  and  $\gamma$  rays\*\*) of mesothorium are for the most part derived from mesothorium II. From these the radio-thorium (Hahn 1905) is formed; it may also be obtained from old mesothorium. Its  $\alpha$  rays have not as yet attained special significance. It is, however, of importance as the producer of thorium X, which has, like mesothorium, grown in therapeutic interest during the past year. Thorium X was discovered in 1902 by Rutherford. The decomposition products

Dixon, British Medical Journal 1898, II., p. 1060.

\*) By half value period is meant the time in which half the substance is transformed or decomposed into other substances.

\*\*) Compare Merck's Report 1911, p. 316.

of thorium, which have been named, cannot be distinguished chemically from one another, but they can be distinguished physically by their different kinds of rays and by their half value times.

	Rays	Half value periods
Thorium	$\alpha$	about 30 milliards of years
Mesothor I	—	5.5 years
Mesothor II	$\beta$ , $\gamma$	6.2 hours
Radiothor	$\alpha$	2 years
Thorium X	$\alpha$	3.6 days.

Other active components of thorium X are thorium emanation, thorium A, thorium B, thorium C and thorium D, which collectively send forth  $\alpha$ ,  $\beta$  and  $\gamma$  rays and all of which represent short-lived elements of high biological effect. Details may be found in an article by J. Plesch, L. Karczag and B. Keetman, which can only be referred to here.

**Mesothorium.** Besides the observers mentioned last year, the following authors have also reported upon the therapeutic employment of mesothorium:

V. Czerny and A. Caan, Münchener medizinische Wochenschrift 1912, No. 14, p. 737.  
 W. Friedländer, Berliner klinische Wochenschrift 1912, No. 15, p. 696.  
 — Deutsche medizinische Wochenschrift 1912, No. 31, p. 1450.  
 Wichmann, Verhandlungen des Lupusausschusses des deutschen Zentralkomitees zur Bekämpfung der Tuberkulose 1911, Berlin.  
 A. Bickel, Deutsche medizinische Wochenschrift 1912, No. 13, p. 625.  
 — Berliner klinische Wochenschrift 1912, No. 17, p. 777.  
 Flemming, Deutsche medizinische Wochenschrift 1911, No. 35, p. 1600; 1912, No. 7, p. 339.  
 O. Hertwig, Sitzungsberichte der kgl. preußischen Akademie der Wissenschaften 1911, p. 844.  
 C. Hahn, Radium in Biologie und Heilkunde 1912, Vol. 1, p. 189.  
 — Therapeutische Monatshefte 1912, No. 5, p. 357.  
 F. A. W. Kröner, Nederlandsch Tijdschrift voor Geneeskunde 1912, p. 1555.  
 A. Sticker, Münchener medizinische Wochenschrift 1912, No. 31, p. 1740. — Berliner klinische Wochenschrift 1912, No. 49, p. 2302 and No. 50, p. 2360.  
 A. Pinkuss, Deutsche medizinische Wochenschrift 1912, No. 38, p. 1777. Chlumsky, Casopis lekaruv ceskych 1912, No. 41.

Czerny obtained the same effects by external radiation of malignant tumours with mesothorium as had been observed

by the employment of radium. The superficial action of mesothorium even appears to be more vigorous, for if the filters used were too weak, severe ulceration was occasionally produced, which, however, soon healed. This action took place more rapidly than with radium and is probably due to the soft  $\beta$ -rays of mesothorium. For superficial ulcers, angioma, lupus and keloids, mesothorium is, according to Czerny, perhaps superior to radium; for lupus and angioma, according to the author's experiments, soon diminished in size and healed over. Carcinomata and sarcomata, on the other hand, were more resistant.

In recurrences of mammary carcinoma, mesothorium was applied as follows: the capsule containing the mesothorium was applied to the nodules for from several hours up to 24 hours by means of a 4 to 8 fold tinfoil filter or by a lead filter 1 to 3 mm. in thickness. By this method the preparation did not act so deeply as when unfiltered rays were employed, which sometimes caused considerable burning of the skin, but at the same time brought about the disappearance of the nodules. Besides the disappearance of the nodules, the pain is alleviated in some patients.

In carcinoma of the face, mesothorium treatment was applied without filtration of the rays, and in 4 cases among 6 patients the process was found to be favourably influenced. The treatment of carcinomata of the oesophagus presented greater difficulty. The mesothorium was introduced in a little silver tube by means of a suitable sound and was left in contact with the affected part for as long as two hours. In four cases the author obtained marked improvement. Carcinomata of the tongue and other carcinomata, especially branchial carcinomata, sometimes reacted well to applications of mesothorium. It was also successful up to a certain point in sarcomata and in one endothelioma, but it failed in 8 cases of lymphosarcoma.

According to Pinkuss, good results may be obtained by mesothorium radiation in inoperable cases of carcinoma of the uterus, the vagina or the vulva, provided the ulceration has not extended too greatly in depth. Like Czerny, Pinkuss is also in favour of the combination of radiation therapy with other methods of employment of radio-active substances, as for example the intravenous, intratumoral or subcutaneous application of thorium X, drinking cures with thorium X, and

finally other measures and medications recognised as therapeutically useful. (Compare below under Thorium X.)

In radiation by mesothorium, Sticker observed after a short time redness and itching of the skin, a few days later vesicle formation, and finally vesicle formation and ulceration. About a month is required for a complete cure. In tumours severe inflammatory irritation of the connective tissue occurs and the tumour cells are affected later. Mesothorium radiation was successful in a case of sarcoma, a recurrence of a laryngeal carcinoma, an angiosarcoma of the upper jaw, a carcinoma of the pharynx, in papillomata, clavi, cancroids and a case of psoriasis. A rectal carcinoma which had grown into the vagina was rendered operable, an epithelial covering was formed over an enucleated carcinoma of the uterus and an extensive carcinoma of the rectum was got rid of, except for small nodules. Among cutaneous tumours, angioma of adults are most resistant.

It is not possible at present to give exact instructions as to the duration of radiation and the amount of protection necessary for the healthy skin in the neighbourhood of the affected parts, as these depend upon the strength and quantity of the preparation and the kind of filter used. Thus some authors consider that the skin should be protected by coverings of lead, others believe that the mica seal of the mesothorium capsule affords ample protection. Some accounts of the modification of the action of mesothorium rays when different filters are used are given by Friedländer, who obtained satisfactory results in a number of skin diseases. The author also points out that by means of mesothorium radiation uterine haemorrhage can be checked or reduced to normal in uncomplicated cases. He states that the necessary technique is simpler and requires less time than is the case with treatment by X rays. He found that the organs (myomata, ovaries) of elderly women, who were approaching the menopause, were especially radio-sensitive. In these cases the effect upon even severe haemorrhages, in the presence of large myomatous tumours, was often surprising and even surpassed the brilliant results obtained by Röntgen therapy. Before undertaking treatment by radio-active substances, a careful examination should be made, especially for the possible presence of new growths, as these require surgical treatment.

Thorium X. The biological and therapeutic action of thorium X has been discussed by the following authors:

Plesch Karczag and Keetmann, Zeitschrift für experimentelle Pathologie und Therapie 1912, Vol. 12, p. 14.  
Th. A. Maas and J. Plesch, ibid. p. 85.  
A. Pappenheim and J. Plesch, ibid. p. 95.  
J. Plesch, Berliner klinische Wochenschrift 1912, No. 49, p. 2305; No. 16, p. 739.  
A. Pinkuss, Deutsche medizinische Wochenschrift 1912, No. 38, p. 1779.  
Czerny and Caan, Münchener medizinische Wochenschrift 1912, No. 14, p. 741.  
A. Bickel, Berliner klinische Wochenschrift 1912, No. 17, p. 777; No. 28, p. 1322.  
Kenji Kojo, ibid. p. 779.  
Minami, ibid. p. 781.  
Orth, Allgemeine medizinische Zentralzeitung 1912, No. 18, p. 233.  
J. Plesch, Berliner klinische Wochenschrift 1912, No. 20, p. 930.  
F. Gudzent, Berliner klinische Wochenschrift 1912, No. 20, p. 933; No. 38, p. 1785.  
Hirschfeld and Meidner, Berliner klinische Wochenschrift 1912, No. 28, p. 1343.  
G. Klemperer and H. Hirschfeld, Therapie der Gegenwart 1912, No. 8, p. 337.  
W. Falta, A. Kriser and L. Zehner, Medizinische Klinik 1912, No. 37, p. 1504. — Wiener klinische Wochenschrift 1912, No. 12, p. 439.  
H. Löhe, Virchows Archiv 1912, Vol. 209, p. 156.  
Nagelschmidt, Deutsche medizinische Wochenschrift 1912, No. 39, p. 1830.  
A. v. Domarus and V. Salle, Berliner klinische Wochenschrift 1912, No. 43, p. 2035.  
K. Herxheimer, Münchener medizinische Wochenschrift 1912, No. 47, p. 2563.  
Nowaczynski, Strahlentherapie 1912, I., p. 342.  
Falta and Zehner, Wiener klinische Wochenschrift 1912, No. 50, p. 1969. — Berliner klinische Wochenschrift 1912, No. 52, p. 2444.  
E. Prado-Tagle, Berliner klinische Wochenschrift 1912, No. 52, p. 2446.

In the literature mentioned above, a large number of results are published which deal with the action of thorium X, and which are in part contradictory. I shall therefore pass over those results which attempt to explain the action on respiration, circulation, ferments, metabolism, bacteria, etc., and shall confine myself to those results which have been furnished by therapeutic or clinical investigation. For the sake of simplicity, a brief abstract will be given of the entire subject matter, arranged according to the indications of thorium X therapy.

**O b e s i t y.** In constitutional obesity, Plesch, Karczag and Keetman succeeded in reducing the weight considerably in many cases by comparatively small doses, or after 2 or 3 administrations of 0·05 to 100 electrostatic units in the course of 8 to 10 weeks. They attribute this less to a loss of water from the organism than to the melting away of the body-fat. But the same effect was not obtained in every case; the authors also met with cases in which the therapy partially or entirely failed.

**A r t h r i t i s u r i c a.** Gudzent formerly stated that uric acid, under the influence of radium emanation, passed into a more soluble form, but this statement was afterwards contradicted by Knaffl-Lenz and Wiechowski. Now thorium X, according to recent investigations, appears to possess this property, which is wanting in radium. Thus Falta and Zehner found that an aqueous suspension of uric acid was coloured yellowish under the influence of thorium X and that the uric acid gradually went into solution. This result found confirmation in a severe case of gout; the authors administered to the patient by mouth an aqueous solution of thorium X in doses of 30 E. U.\* each, 3 times a day, with the result that the patient's condition was considerably improved, the pains and swellings disappearing almost entirely. Plesch, Karczag and Keetman also used thorium X in a number of cases of gout and found that the disease was always favourably influenced. 20 to 30 E. U. administered weekly sufficed to effect the elimination of uric acid, to relieve the pains and to increase the mobility or to alleviate the rigidity of the joints to a certain extent.

**A n æ m i a , p e r n i c i o u s a n æ m i a , l e u k æ m i a .** In these indications, the administration of thorium X deserves special consideration. Klemperer and Hirschfeld obtained symptomatic cures, some of which were extraordinary, in 75 p. c. of cases of leukæmia (lymphatic and myeloid). The leucocyte count was reduced to normal or below normal, the spleen and lymphatic glands were diminished in size, the general health was improved and leukæmic changes of the fundus oculi were influenced by this treatment. The authors were also successful in several cases of pernicious anaemia. In 3 out

\*) E. U. = Electrostatic Unit. 1 E. U. = 1000 M. U. (Mache Unit.)

of 7 cases the number of red blood corpuscles and the haemoglobin content were increased, while 4 cases remained unaffected. As a result of these experiments, the authors recommend that thorium X should only be resorted to if treatment by arsenic and antimony has failed. The experiments of Falta, Krieger and Zehner, and those of Nagelschmidt, Nowaczynski, Plesch and his assistants also show that treatment by thorium X may have a favourable influence on lymphatic and myeloid leukæmia. Falta gave subcutaneous or intramuscular injections of 50,000 to 1,000,000 M. U. at intervals of 2 to 3 days with the same beneficial results as were obtained by Klemperer and Hirschfeld, Plesch administered 250 and 875 E. U. internally and 300 to 600 intravenously in myeloid leukæmia, and 500 to 3000 E. U. intravenously in lymphatic leukæmia.

Plesch, Bickel and Prado-Tagle discuss the action of thorium X in pernicious anaemia. According to the experiments carried out hitherto, it appears to be better than in leukæmia. Tagle reports a case in which he gave 50 E. U. a day, divided into 3 portions, after meals. After the first 3 days the patient began to feel better, while the appetite and shortness of breath were improved. The attacks of vertigo disappeared after six weeks and after ten weeks the patient was able to return to work. The blood picture was practically normal. According to Bickel, striking and lasting improvement can be obtained in pernicious anaemia both by the thorium X drink cure and by injections of thorium X. Plesch observed an influence on the number of white blood corpuscles after the (intravenous) injection of 100 E. U., and he therefore gave smaller amounts as "stimulant doses", 50 E. U. as a maximum stimulant dose. In his experience, the body should be exposed to constant stimulation, which may be attained by the frequent application of thorium X. But thorium X may be administered internally with equally good results.

Carcinoma, Sarcoma. The treatment of malignant tumours by thorium X is reported upon by Czerny, Herxheimer, Pinkuss and others. As it is still in the early stages, no definite conclusion can as yet be drawn as to its value, but the reports of the various observers show that good results may be expected from thorium X therapy. Czerny treated 36 cases (31 carcinomata and 5 sarcomata) by means

of intravenous and intratumoral injections, using a solution corresponding to about 1 to 3 millions of M. U. to 1 c. c. The intratumoral injection of these doses was on the whole well tolerated. After 24 hours, swelling and para-tumoral oedema occurred, and these symptoms disappeared after 72 hours. The swelling was usually followed by a diminution in size of the tumours. But the intravenous injection of 1 c. c. of the thorium X solution mentioned above occasionally gave rise to vomiting, loss of appetite and vertigo; there was, however, no disturbance of the vital organs and no albuminuria. After intravenous injection, the author also frequently observed swelling of the tumour, which was followed by shrinking and induration. The tumours were frequently diminished in size and the subjective condition improved. According to Czerny, no positive statement can as yet be made as to the therapeutic value of thorium X, but he believes that a certain significance cannot be denied to thorium X treatment in combination with external mesothorium radiation. Pinkuss tried this combined treatment; he not only gave thorium X by intravenous and intratumoral injection, but also internally. Except when the dosage was too high he observed no injury of the organism. He administered on an average 1 million M. U. intravenously and prescribed drinking cures of 50,000 M. U. a day, to be continued for weeks. In this way he several times succeeded in bringing the disease to a standstill for prolonged periods in cases of recurrent carcinoma, which no longer reacted to direct radiation and to surgical procedures. He also combined thorium X therapy with the administration of pancreatin. The author does not as yet offer a definite opinion as to the value of this treatment, but he remarks that during the treatment he has frequently observed lasting improvement of the general health and apparent strengthening of the debilitated organism.

Herxheimer describes a case of sarcoma which he cured by means of thorium X. The case was one of multiple sarcomata of the skin, the prognosis of which was very grave, for these cases, according to the author's experience, usually end fatally. He therefore injected a dose of 1000 E. U. at intervals of a week, without observing the secondary effects described by Czerny. After 7 injections all the nodules had practically disappeared, as had also the pigmentary hypertrophy remaining in the position of the nodules cured by

previous injections. The skin over the entire body and the mucous membrane of the mouth and pharynx were normal.

**Scleroderma.** Plesch treated a case of scleroderma by means of thorium X; he injected a dose of 100 E. U. The swelling of the joints subsided and the mobility was improved.

**Infective diseases.** Plesch offers a few observations on this subject. It cannot yet be said with certainty whether thorium X offers a prospect of marked success in tuberculosis, pneumonia, sepsis and suppuration in accessory cavities. Acute muscular and articular rheumatism, however, are certainly benefited by thorium X therapy. The method of application does not appear to be a matter of importance in these cases. The author recommends that the patient be given small doses of 10 to 30 E. U. at intervals of 2 to 3 days. Relapses, which may occur after the treatment, are improved by further administration of the preparation.

**Diseases of the circulatory system.** Thorium X may also come into consideration as a means of lowering the blood pressure. Although, like other drugs employed to lower the blood pressure, it is not always efficacious, it has, according to Plesch, the advantage of being effective in comparatively low activities, of giving rise to no injurious by-effects and of apparently acting as a direct sedative to the circulation. Plesch assumes that thorium X increases the elasticity of the cardio-vascular system and permanently lowers the blood pressure. He specially recommends it for relative and absolute cardiac over-exertion. In various stenocardiac attacks (*angina pectoris*) the author attained noteworthy results by the intravenous injection of 100 to 1300 E. U.

Reference may also be made to a communication by Falta, Kriser and Zehner. These authors gave subcutaneous and intra-glandular injections of large doses, up to 1,000,000 M. U. of thorium X, in tuberculous lymphadenitis. The results were, in part, highly encouraging, but the painful infiltrations occurring after such large doses necessitated the reduction of the doses to not above 300,000 M. U. If larger doses were required, the dose mentioned above was injected in two places at the same time. However, the authors were able to convince themselves later that such large doses were not necessary, for the cases which react to thorium X do so to small continuous doses. Thus, doses of 200,000 to 300,000 M. U. are suffi-

cient. A case reported by Orth shows that too large doses may prove dangerous; an adult woman (suffering from chronic arthritis) was given, in the course of 16 days, 3 injections of thorium X in amounts of 900,000, 550,000 and 3,000,000 M. U. The last and strongest injection was followed after 3 days by vomiting and abdominal pain, and after 4 days more by loss of strength, which led to death on the tenth day after the last injection. According to Gudzent, doses up to 4,000,000 M. U. have been borne without causing marked secondary symptoms, but caution is necessary with large doses. Löhe concludes, after experiments on animals, that a dose of 1,000,000 M. U., given at intervals of a week, is harmless. But, according to Plesch, there are many points to be considered in the dosage of thorium X. Thus, old people and men can stand more than young people and women. At any rate, a dose of 1000 E. U. should very rarely be exceeded. The patient must be carefully watched, and if diarrhoea or abdominal pain occur, the medication must be discontinued at once. To avoid injury of the intestine by prolonged retention of the excreted thorium in the bowel, the application of thorium may be followed by aperients, in order to hasten excretion. But for leukæmia Plesch is in favour of large doses, as small ones are ineffective. In other diseases small doses suffice, for example 0.05 to 100 E. U. in gout and rheumatism.

### Methylene Blue.

On account of its bactericidal action and its harmlessness, methylene blue has been suggested by various authors for the treatment of affections of the eyes. Bichon especially recommends it in 0.1 p. c. aqueous solution for ulcers and abscesses of the cornea and has obtained very good results by its use.

As a test for aceto-acetic acid in the urine, Béla v. Ondrejovich has worked out a test which is said to have several advantages over Gerhardt's reaction\*). The new test depends upon the fixation of iodine by aceto-acetic acid

Bichon, Archives médicales d'Angers 1912, 20<sup>th</sup> March.

Ondrejovich, Deutsche medizinische Wochenschrift 1912, No. 30, p. 1413.

\*) Compare Sturdy Sinnat, Merck's Report 1910, p. 251.

and the employment of methylene blue as an indicator for free iodine. If 5 drops of urine are mixed with 5 drops of acetic acid (50 p. c.), and one drop of 0·2 p. c. methylene blue solution is added, a mixture is obtained of a pronounced blue colour, failing which another drop of methylene blue solution should be added. On the addition of 4 drops of iodine, the mixture turns red. But in the presence of aceto-acetic acid it turns blue or green again within one minute. The aceto-acetic acid absorbs the iodine and decolorises it with formation of mono-iodo-aceto-acetic acid. At the same time the lightly bound iodine-methylene blue gives off the iodine, thus becoming methylene blue with its original blue coloration. If 5 c. c. of urine contain sufficient aceto-acetic acid to bind the iodine of the tincture of iodine which has been added, this combination takes place instantaneously and the methylene blue retains its blue colour. With a little practice it will be possible to tell whether aceto-acetic acid is present on the addition of the first drop of tincture of iodine, from the rapidity with which combination takes place. Other substances which combine with iodine only do so very slowly, at any rate much more slowly than does aceto-acetic acid.

The above described test can be rapidly carried out and is reliable; it is not interfered with by other substances, such as salicylic acid, antipyrine, acetone, etc., and is more sensitive than the customary tests.

E. Herzfeld reports upon a quantitative estimation of glucose in the blood or blood serum. It depends upon the precipitation of albuminous substances by meta-phosphoric acid and the titration of the filtered solution with an alkaline solution of methylene blue. The following solutions are employed:

1. Aqueous solution of methylene blue 1:100 000,
2. 20 p. c. caustic potash solution,
3. 10 p. c. meta-phosphoric acid,
4. 0·1 p. c. solution of glucose.

To a measured amount of glucose solution 0·5 c. c. of caustic potash solution is added; the mixture is heated almost to boiling over an asbestos plate and the methylene blue solution is added drop by drop from a burette until the colour remains

permanent. According to Herzfeld, 1.5 c.c. of methylene blue solution will on an average be required. When the correspondence between the methylene blue solution and glucose has thus been established, 5 c.c. of blood or blood serum are mixed with 15 c.c. of meta-phosphoric acid, filtered after 10 minutes and the filter and precipitate washed with meta-phosphoric acid. The filtrate is neutralised with caustic potash solution, 0.5 c.c. of caustic potash solution are added, and it is titrated with methylene blue solution as described.

### Methyl-Strophanthin.

This new preparation, first prepared by Herzig by methylising strophanthin, has been thoroughly investigated by Schapkaiz, together with other strophanthins, according to the method of Fränkel; he came to the following conclusions: The strength of action of methyl-strophanthin when applied subcutaneously to cats lies between that of amorphous strophanthin (Böhringer) and that of crystalline strophanthin (Thoms). A single doses of 0.00003 gramme of crystalline strophanthin causes the animal to become ill; of amorphous strophanthin (Böhringer) the cat can tolerate 0.00008 gramme a day without showing any signs apart from the therapeutic action. But methyl-strophanthin can only be given several times in succession in doses of 0.00005 gramme at intervals of 24 hours, while a daily dose of 0.000075 gramme causes vomiting already after the second administration. Methyl-strophanthin, like the digitalis substances, shows cumulative action. In this respect it lies between the two other strophanthins which have been mentioned. Its after-effect is more prolonged than that of crystalline strophanthin, but it is not like the latter of the digitoxin type; in crystalline strophanthin, as in digitoxin, the difference between an effective and a fatal dose is slight, so that it is not possible to achieve pure therapeutic action by a single dose; but this is readily done with amorphous strophanthin (Böhringer) and with methyl-strophanthin. The prolonged after-effect of methyl strophanthin, even after single doses, as observed by Schapkaiz, appears to justify the trial of the new drug in man. It may be noted that methyl-strophanthin is not yet, to my knowledge, on the market.

### Microscopic Stains.

A. Schott has elaborated a simple process for the polychromic staining of formed components of the urine, which does not take longer than the examination of unstained sediments. For this purpose are required: a solution of 5 grammes of aniline blue in water, and a solution of 2·5 grammes of eosin in 100 grammes of glycerin with the addition of 5 p. c. carbolic acid. About 10 c. c. of the urine to be tested are mixed in a centrifuge tube with 3 drops of aniline blue solution and 6 to 8 drops of eosin solution. After centrifuging, the sediment, which has become stained, is examined under the microscope. For the demonstration of casts fresh urine should be used, which is passed in the presence of the doctor, for in the author's experience these delicate structures may no longer be visible after a few hours.

For staining gonococci by Gram's method, V. Jensen has for years only used a 0·5 p. c. solution of methyl violet 6 B, a 0·1 p. c. solution of neutral red and a solution of 1 gramme of iodine and 2 grammes of potassium iodide in 100 grammes of water. A mordant, such as aniline or carbolic acid, is, in his experience, not required and necessitates the constant preparation of fresh reagents, whereas the solutions mentioned above keep for a long time, if necessary, in a concentrated form. His procedure is briefly as follows: A thin layer is spread over the slide. — It is dried in the air. — Passed through the flame. — When cool, the 0·5 p. c. aqueous solution of methyl violet is poured on and after a quarter to half a minute is washed off with the iodine solution. — A fresh quantity of iodine solution is poured on and after half to one minute is washed off with absolute alcohol. — It is decolorised with absolute alcohol. — Neutral red solution is poured on and after a quarter to half a minute is washed off with water. — It is dried in the air. This modification of Gram's method may be used for staining gonococci and for the staining of other bacteria.

The rapid staining of spirochæta pallida in the tissue is, according to H. Nakano, carried out as follows. Small

Schott, Münchener medizinische Wochenschrift 1912, No. 4, p. 182.

Jensen, Berliner klinische Wochenschrift 1912, No. 35, p. 1663.

Nakano, Deutsche medizinische Wochenschrift 1912, No. 9, p. 416.

fragments of tissue are fixed for 10 to 20 minutes in 10 p. c. formalin solution and are then cut into sections 1 to 2 mm. in thickness; they are placed in 95 p. c. alcohol (3 to 5 hours) and then in water (10 minutes), and are then transferred to a 1.5 p. c. solution of silver nitrate at 50° C. for 4 to 5 hours. They are then treated at the same temperature with a solution of 3 grammes of pyrogallol and 5 grammes of 10 p. c. formalin in 100 grammes of water. Finally they are treated consecutively with 95 p. c. alcohol, absolute alcohol and xylol and are embedded in paraffin. If the investigation of hereditary syphilis, broad condylomata and hard chancre is begun in the early morning, it is possible to ascertain by the following evening whether or not the tissue contains spirochetes.

Two methods of testing for diphtheria bacilli have been described by C. Ponder and Conradi. The stain used by Ponder consists of a solution of 0.02 gramme of toluidin blue, 1 c. c. of glacial acetic acid and 2 c. c. of alcohol in 97 c. c. of water. Films from the culture and from the throat are examined in hanging drops by artificial light. The characteristic feature of diphtheria bacilli is a blue coloration with red granules. Sarcinae and yeast are similarly stained, but may readily be distinguished from diphtheria bacilli. This method has the advantage over the methylene blue stain of furnishing a double stain. It enables an immediate diagnosis to be made in over 50 p. c. of cases of acute diphtheria. A negative result of the stain is of no diagnostic value. The nutrient medium described by Conradi appears to furnish better results. A mixture of 1000 c. c. of water, 10 grammes of meat extract, 5 grammes of common salt, 20 grammes of dried peptone and 6 grammes of calcium bimalate is heated for half hour in a steamer, filtered, 1 p. c. glucose added and one part of this mixture stirred up with 3 parts of fresh ox serum. To 100 parts of the mixture thus obtained, 2 c. c. of a 1 p. c. solution of potassium tellurate are added and it is allowed to set in a Petri dish. On this nutrient medium diphtheria bacilli are coloured black, while the potassium tellurate checks the growth of other bacteria from the mouth.

**Mistletoe.**

The action of mistletoe on the circulation is due, according to A. Selig, to two saponin-like glucosides, found years ago in this plant by Chevalier. The investigations of Gaultier and Chevalier, and also those of Fubini and Antonini, show that the intravenous application of the drug causes a not inconsiderable decrease in the blood pressure. Mistletoe also has a diuretic effect, which Chevalier considered to be due to the action of the glucoside on renal secretion. It is specially noteworthy, because most of the drugs at present in use for lowering blood pressure exert no such action on the kidneys.

Selig's experiments with mistletoe leaves and preparations on the whole confirmed the statements of the above named observers. Intravenous injection caused a transient fall of blood pressure in rabbits, dogs and cats, before and during which the efficacy of adrenalin, of section of the vagus, stimulation of the central end of the vagus and of asphyxia remained undiminished. But no marked action on the heart or respiration was observed. The prolonged administration of mistletoe preparations by mouth effected no alteration in the blood pressure, but usually increased diuresis could be observed\*).

From the American mistletoe, *Phorodendron flavescens* Nutt. (belonging, like *Viscum album*, to the family of Loranthaceæ) A. C. Crawford isolated a crystalline substance, which is said, like adrenalin, to cause a permanent rise of blood pressure. It is presumably nearly related chemically to phenylethylamine. The American mistletoe has not been extensively used in therapeutics. In its native land (Mexico, California) it is said, according to older communications by Möller, Rusby and Long, to have been tried in uterine haemorrhage and for the production of labour pains. Long

Selig, Medizinische Klinik 1912, No. 24, p. 991.

Chevalier, Comptes rendus de la société de biologie 1908, p. 2.

Gaultier-Chevalier, ibid. 1907, p. 941. — Gazette des hôpitaux 1907, No. 119. — Nouveaux remèdes 1907, p. 529.

Fubini-Antonini, Annali di farmacologia sperimentale e scienze affini, Vol. 12, pag. 450.

\*) Compare Merck's Report 1907, p. 257.

Crawford, Journal of the American Medical Association 1911, Vol. 57, p. 865.

Möller, American Journal of Pharmacy 1882, Vol. 55, p. 421.

Rusby-Long, Druggist Bulletin 1889, Vol. 3, p. 255.

states that he has obtained the same action with 4 grammes of the fluid extract as with ergotin.

### Morphine Hydrochloride.

The tonic and regulating action of morphine in cardiac disease is fully discussed by Siebert. He considers it a curative drug, but not a cardiac poison and states that it is specially indicated for the relief of troublesome symptoms and sensations and the elimination of excessive muscular work of the heart. It is of great service even when digitalis fails. The fact that when digitalis fails to act, morphine may restore its efficacy is of special significance. The regulation of cardiac action brought about by morphine apparently depends upon its sedative influence on the central and peripheral cardio-vascular nervous system, or upon the increased tone of the vagus, which improves the cardiac action and has a favourable influence upon the circulation.

According to V. Brun, morphine may be employed more than has hitherto been the case in operations on children, for the author finds the drug to be relatively harmless and very well tolerated, even by babies. Being a uniform substance, of which an exact dose can be given, morphine is superior to other hypnotic and sedative drugs. It is best to regulate the dosage according to the body-weight and to begin with a daily dose of 0.5 milligramme by mouth for every kilogramme of weight. By enema the corresponding dose will be 0.3 milligramme, and subcutaneously 0.1 milligramme. Brun reports 300 cases of children aged from 4 months to 12 years, who received injections of morphine to effect analgesia for operations before inducing anaesthesia. The results showed that the effect produced by the morphine corresponded to the analgesic stage usually obtained with other narcotic drugs. In operations on the head in babies, the injection of morphine in the dose suggested sufficed by itself to effect the necessary amount of analgesia. The author has also successfully used ethyl chloride in order to convert the analgesic stage into complete anaesthesia. Older children were given one or two further injections of morphine to act as a sedative after operations, especially after orthopaedic opera-

Siebert, Beihefte der Medizinischen Klinik 1912, No. 6.

Brun, Gazzetta degli ospedali e delle cliniche 1912, No. 46. —

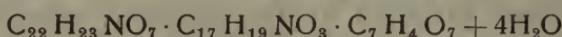
Klinisch-therapeutische Wochenschrift 1912, No. 33, p. 967.

tions. By the combination of morphine injections with general anaesthesia, the morphine has a favourable effect on cardiac activity. On awakening from the anaesthesia, the author has observed flushing of the upper half of the body, caused by paresis of the vessels. It is stated that 1 centigramme of morphine may be given to babies without danger and with satisfactory results.

In order to avoid the secondary effects of morphine, Overlach has tried a combination of morphine with valerianic acid and other medicaments, so-called "Trivalin". It is a solution of 3.87 grammes of morphine valerianate, 0.74 gramme of caffeine valerianate and 1.012 grammes of cocaine valerianate in 200 c.c. of water. Thus 1 c.c. contains 0.01935 gramme of morphine valerianate, 0.0037 gramme of caffeine valerianate and 0.00506 gramme of cocaine valerianate, which corresponds to a medium dose. The author describes this combination as detoxicated morphine, the toxic effects of the morphine being paralysed by the chemical antagonism of the bodies present, which are bound to valerianic acid. It is said to offer the advantage that vomiting does not occur, nor do symptoms of paralysis of the heart and of the respiratory centre. The indications for the preparation are the same as those of morphine.

### Narcophin.

A double salt consisting of one molecule of morphine and one molecule of narcotine with one molecule of divalent meconic acid is put on the market under the name of narcophin. This morphine-narcotine-meconate, having the chemical formula



contains an amount of morphine corresponding to 38 p.c. of morphine hydrochloride.

The investigations of W. Straub, O. Herrmann, P. Pott, B. von Issekutz and H. Caesar led to the intro-

Overlach, Zentralblatt für innere Medizin 1912, No. 18, p. 422.

Straub, Biochemische Zeitschrift 1912, Vol. 41, p. 419. — Münchener medizinische Wochenschrift 1912, No. 28, p. 1542.

Herrmann, Biochemische Zeitschrift 1912, Vol. 39, p. 216.

Pott, Biochemische Zeitschrift 1912, Vol. 42, p. 67.

Issekutz, Pflügers Archiv 1912, Vol. 145, p. 415.

Caesar, Biochemische Zeitschrift 1912, Vol. 42, p. 316.

duction of this preparation. For Straub found that narcotine, although the least efficacious alkaloid of opium, is capable of strengthening the action of morphine. But as narcotine is a relatively indifferent body, it can be used for rendering the action of morphine more powerful, while dispensing with the other more toxic alkaloids of opium. Straub also established the relations in which the morphine-narcotine combination represents the highest efficacy, and this led to the preparation of morphine-narcotine-meconate. According to Straub, narcophin has the advantage over morphine of acting more powerfully than the latter, while having less effect upon the respiratory centre.

According to Zehbe, the action of narcophin is somewhat weaker than that of an equal dose of morphine; but the dose may be increased twofold, as the secondary effects which usually occur on administration of narcotics, such as headache, numbness and vomiting, remain practically absent when narcophin is used. Narcophin, however, retards intestinal peristalsis and thus forms a substitute for opium. For internal administration, the author gave a dose of 15 to 30 drops of a 3 p. c. solution of narcophin 3 times a day; its action was manifest in  $\frac{3}{4}$  to 1 hour, whereas it occurred in 15 minutes after the subcutaneous application of 1 c. c. of this solution (= 0.03 gramme).

Schlümpf prescribed narcophin in gynaecological practice as an analgesic and a soporific (1 c. c. of the 3 p. c. solution given subcutaneously), and in combination with scopolamine as a preliminary narcotic before inducing inhalation anaesthesia, or lumbar or sacral anaesthesia. For this purpose he used 0.03 gramme of narcophin and 0.0003 gramme of scopolamine hydrobromide given 3 and  $2\frac{1}{2}$  hours before the operation. To elderly and febrile women he only gave half this dose. The action sets in later than that of morphine, but the narcotic effect is said to be more potent and to last longer than after the use of scopolamine-morphine.

Stalewski gave doses of 0.03 gramme of narcophin with satisfactory results in painful conditions, such as colic, gall stone colic, cardiospasm, painful labour pains and in primary

Zehbe, Münchener medizinische Wochenschrift 1912, No. 28, p. 1543.

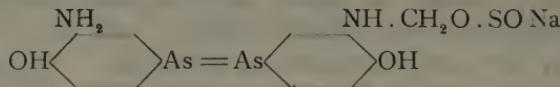
Schlümpf, Münchener medizinische Wochenschrift 1912, No. 28, p. 1544.

Stalewski, Therapie der Gegenwart 1912, No. 11, p. 507.

uterine inertia. According to his experience, the preparation should also prove useful in the cure of the morphine habit.

### Neosalvarsan.

Neosalvarsan is the sodium salt of dioxy-diamino-arseno-benzol-monomethane-sulphinic acid



a yellowish powder, having a peculiar odour and dissolving in water with a neutral reaction. It contains 21.7 p. c. of arsenic (salvarsan 31 p. c.). It has the advantage over salvarsan of being more easily administered on account of its solubility in water. Otherwise practically the same technique applies as for salvarsan. For its solution freshly distilled, sterile water which is free from bacteria must be used. The solution must not be warmed nor shaken and it must not be left to stand for long, as it is more easily oxidised than salvarsan solution and may then give rise to very undesirable secondary effects. Thus, the solution required for intramuscular or intravenous injection should always be freshly prepared and used at once. For intramuscular injection a 5 p. c. aqueous solution is used, and 0.6 p. c. for intravenous application. Subcutaneous injection is not advised, as it gives rise to pain and infiltrations.

The indications for neosalvarsan are the same as those of salvarsan. It has been chiefly tried for syphilis, but also in malaria, framboesia, relapsing fever, etc. The first question to decide in suggesting neosalvarsan as a substitute for salvarsan is whether the new preparation is more efficacious and gives rise to less harmful secondary effects. Opinions are, however, at variance on this score. The majority of authors are satisfied with the action of the drug in syphilis and consider it equivalent to that of salvarsan, but other views have been expressed. Thus Levy-Bing, Dureaux, Spillmann, Boulangers, Wolff, Mulzer, Gennerich and Bettmann consider neosalvarsan to be, on the whole, less efficacious, while Schreiber, Hudelo, Montlauer and Bodineau, Queyrat and Bouttier consider it more efficacious in one direction or another. Krefting found that the action of neosalvarsan on the clinical symptoms is not inferior to that of salvarsan, but that it is less effective in ren-

dering the Wassermann reaction negative, and this on the whole tallies with Gennerich's experiences.

On account of the solubility of neosalvarsan and of its being unnecessary to neutralise the preparation with caustic soda, as is required with the solution of salvarsan, secondary effects are usually absent (Schreiber, Touton, Wechselmann). But caution is necessary, as Kall and Simon have observed serious secondary effects, such as drug rash with threatening secondary symptoms\*). Busse and Merian record a fatal case. It was therefore suggested that small doses be given at long intervals and in this manner neosalvarsan produces no worse, but rather slighter secondary effects than salvarsan.

With regard to dosage, Schreiber at first gave up to 1.5 grammes to men, up to 1.2 grammes to women, 0.15 gramme to children, and 0.05 gramme to sucklings, at intervals of 1 to 2 days. But the occurrence of secondary effects caused these doses to be considerably reduced. The author reduced the doses to 0.4 to 0.6 gramme for men, and to 0.3 to 0.5 gramme for women and prolonged the intervals between the injections to a fortnight. The author also advises caution in recent secondary syphilis, for on account of the large number of spirochetes in the meninges, there is danger of the occurrence of cerebral swellings. In meningitis, cerebro-spinal syphilis, tabes and general paralysis, Stühmeyer recommends small initial doses of 0.15 gramme which, if well borne, may gradually be increased at intervals of a week to 0.5 to 0.75 gramme. For intramuscular injection the same doses are given. Schreiber prescribed doses of 0.3 to 0.45 gramme, Gastou 0.45 to 0.75 gramme, Kall 0.7 gramme and Iversen 0.9 gramme. In syphilis of the central nervous system, Wechselmann gave neosalvarsan by lumbar injection without evident disturbance. For this purpose he used 2 to 7 c.c. of a solution 0.15:100.

In veterinary surgery neosalvarsan may also be used in place of salvarsan. Rips dissolved 4 grammes of neosalvarsan in 110 grammes of 0.3 p.c. saline solution (at 25°C.), shaking gently twice. He used this solution for intravenous injection in contagious pneumonia of horses (See also Salvarsan).

\* ) Compare also Gennerich, Bernheim and Emery.

The following is a summary of the neosalvarsan literature:

**Framboesia:**

Sabella, Münchener med. Woch. 1912, No. 52, p. 2885.

**Malaria:**

Iversen, Münchener med. Woch. 1912, No. 29, p. 1606. — Werner, Deutsche med. Woch. 1912, No. 44, p. 2068.

**Relapsing Fever:**

Conseil, Therapeutische Monatshefte 1912, No. 12, p. 879.

**Syphilis:**

Bayet, Journal méd. de Bruxelles 1912, 12<sup>th</sup> Sept. Zentralblatt f. d. ges. Arzneimittelkunde 1912, p. 437. — Bernheim, Deutsche med. Woch. 1912, No. 22, p. 1040. — Bettmann, ibid. 1912, No. 48, p. 2292. — Brocq, Françon, Fernet, Bullet. Soc. Franç. de Dermatol. 1912, July. — Castelli, Deutsche med. Woch. 1912, No. 32, p. 1487 and No. 35, p. 1633. — Darier, Libert, Bullet. Soc. Franç. de Dermatol. 1912, July. — Dohi, Watanabe, Japan, Ztschr. f. Dermatol. u. Urolog. 1912, No. 6. — McDonagh, Brit. Med. Journ. 1912, I., p. 1287. — Duhot, Revue belge d'Urolog. Dermatosyphil. 1912, April. — Fabry, Medizinische Klinik 1912, No. 34, p. 1385. — Gennerich, Berliner klin. Woch. 1912, No. 25, p. 1170; No. 26, p. 1227 and No. 27, p. 1268. — Grünberg, Münchener med. Woch. 1912, No. 29, p. 1607. Deutsche med. Woch. 1912, No. 44, p. 2070. — Grünfeld, Deutsche med. Woch. 1912, No. 25, p. 1176. — Gutmann, Berliner klin. Woch. 1912, No. 31, p. 1467. — Heuck, Dermatol. Woch. 1912, No. 48, p. 1474. — Hudelo, Montlaur, Bodineau, Bullet. Soc. Franç. de Dermatol. 1912, 6<sup>th</sup> June. — Jordan, Dermatol. Ztschr. 1912, No. 19, p. 992. — Iversen, Münchener med. Woch. 1912, No. 26, p. 1436. — Kall, ibid. 1912, No. 31, p. 1710. — Krefting, Berliner klin. Woch. 1912, No. 45, p. 2130. — Kerl, Wiener klin. Woch. 1912, No. 45, p. 1787. — Lévy, Bing, Gazette des hôpital. 1912, No. 66. — Leredde, Bullet. Soc. Franç. de Dermatol. 1912, 6<sup>th</sup> June. — v. Marschalkó, Deutsche med. Woch. 1912, No. 34, p. 1584. — Pinkuss, Medizin. Klinik 1912, No. 33, p. 1361. — Queyrat, Bouttier, Bullet. et Mém. Soc. méd. des hôp. de Paris 1912, p. 589. — Rosenmeyer, Münchener med. Woch. 1912, No. 45, p. 2459. — Schreiber, ibid. 1912, No. 17, p. 905. — Solowjeff, Russkij Wratsch 1912, No. 21, p. 962. — Spillmann, Boulanger, Bullet. Soc. Franç. de Dermatol. 1912, July. — Spitzer, Zentralbl. ges. Therap. 1912, No. 11, p. 561. — Stroscher, Münchener med. Woch. 1912, No. 40, p. 2161. — Stühmer, Deutsche med. Woch. 1912, No. 21, p. 983. Münchener med. Woch. 1912, No. 45, p. 2447. — Touton, Berliner klin. Woch. 1912, No. 24, p. 1118. — Wechselmann, Deutsche med. Woch. 1912, No. 31, p. 1446. Münchener med. Woch. 1912, No. 39, p. 2099, No. 38, p. 1174. — Wolff, Mulzer, ibid. 1912, No. 31, p. 1706.

**Secondary Effects:**

Busse, Münchener med. Woch. 1912, No. 43, p. 2330. — Emery, La Clinique 1912, No. 31. — Kall, Medizin. Klinik 1912, No. 33, p. 1362. — Simon, Münchener med. Woch. 1912, No. 43, p. 2328. — Stern, Dermatol. Woch. 1912, No. 48, p. 1474. — Mayer, Berliner klin. Woch. 1912, No. 35, p. 1662.

**Technique:**

Balzer, Bullet. Soc. Franç. de Dermatol. 1912, 4<sup>th</sup> July. — Gastou, ibid. 1912, 6<sup>th</sup> June. — Schreiber, Münchener med. Woch. 1912, No. 34, p. 1850. — Stephan, Apoth.-Zeitung 1912 No. 61, p. 583.

**Veterinary Medicine:**

Rips, Berliner tierärztl. Woch. 1912, No. 23, p. 405.

**Neuronal.**

After several years' experience of this hypnotic and sedative, M. Seige discusses its therapeutic properties. He has prescribed the preparation in daily doses of 0·5 to 3 grammes ( $7\frac{1}{2}$ —45 grains) in a large number of cases, partly psychiatric and partly nervous. It proved useful in simple insomnia, such as occurs in neurasthenics, hysterical subjects and persons with exaggerated emotions, while it was of less use in neurasthenics, who found particular difficulty in falling asleep. It gave good results also in the vaso-motor disturbances of various neuroses, especially in climacteric disturbances.

In epilepsy, the author never succeeded in diminishing the number of fits by the regular administration of neuronal, although he gave 0·5 gramme ( $7\frac{1}{2}$  grains) 3 times a day for a prolonged period. The only result was a certain amount of drowsiness. But in severe epileptic symptoms the drug proved useful in combination with amylen hydrate. Thus doses of 2 grammes (30 grains) of neuronal and 6 grammes (90 min.) of amylen hydrate brought about prolonged, refreshing sleep in the severe epileptic semi-conscious conditions of a patient who had remained unaffected by large doses of scopolamine. In mentally affected patients, the hypnotic effect of 1 to 2 grammes (15—30 grains) of neuronal was, on the whole, satisfactory; it failed, however, in two excitable cases of senile dementia suffering from motor restlessness; but this might easily happen with other drugs. In maniacs the action of 2 grammes (30 grains) of neuronal was, on the whole,

insignificant, but in fractional doses the medicament led to better results. The majority of excitable patients were markedly tranquillised after 3 days' administration of 0.5 gramm (7½ grains) 3 times a day; it was specially beneficial for those patients who could not be persuaded to enter the continuous bath and had in consequence to be treated with scopolamine. Seige did not observe any serious secondary effects from the use of neuronal; only after its prolonged use did he meet with disturbances of speech and slight disturbances of gait; in 3 cases there was vomiting, several times pathological chemical constituents or formed constituents were present in the urine, in two cases of insanity and in a typical case of cardiac neurosis there was a transient increase in the pulse rate, but in no case was the blood pressure affected.

Seige drew particular attention to a combination of neuronal and acetanilide. He at first administered doses of 1 gramm (15 grains) of neuronal and 0.25 gramm (4 grains) of acetanilide, later doses of 0.5 gramm (7½ grains) of neuronal and 0.5 gramm (7½ grains) of acetanilide. This mixture is said to have a striking effect in severe pains of all kinds, for example in severe headaches of arterio-sclerotic subjects, in inoperable cerebral tumours and in migraine. It did not affect the crises of tabes.

### Neutral Red.

Neutral red (dimethyl-diamido-tolu-phenazin hydrochloride) is a dark, blackish-green powder\*), which dissolves in water, imparting to the solution a crimson colour. The alcoholic solution is fuchsine-red in colour and shows a brownish-red fluorescence. The aqueous solution is coloured blue by hydrochloric acid, while with caustic soda a yellowish-brown precipitate is produced.

The dye is sometimes used for microscopic and analytical purposes\*\*). A new method of employment was described by E. Moro. By means of a neutral red solution human milk can be distinguished from cow's milk, a test which may, under certain conditions, be of importance in institutions for young babies. If to 5 c.c. of milk are added 2 drops of a

\*) Compare Merck's Report 1908, p. 258.

\*\*) Compare Merck's Reagenzien-Verzeichnis.

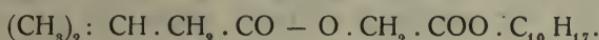
Moro, Münchener medizinische Wochenschrift 1912, No. 47, p. 2553.

1 p. c. solution of neutral red in normal saline solution, cow's milk will be coloured reddish-violet and human milk yellow. It is important that the human milk has not become sour. The reaction must be carried out at the temperature of the room, because human milk kept in an ice-safe shows a red coloration, whereas at the ordinary temperature it is coloured yellow by the reagent. But the appearance of a red coloration does not always necessitate the rejection of the milk. The author suggests the following tests. If a sample of milk has been kept for some time, a small drop of the reagent is placed on the surface of a small teaspoonful of the milk. If there is an immediate formation (without brown transitional shades) of a pronounced reddish-violet colour, the human milk is no longer fit for the nutrition of sucklings. The reaction also serves to detect the addition of 1 part of cow's milk to 10 parts of human milk.

G. Quagliariello and E. d'Agostino use neutral red, together with nitrophenol, as a clinical test for urinary reaction. For their method are required: a solution of 1 grammme of p-nitrophenol in 60 c. c. of alcohol and 940 c. c. of water, and a solution of 0·2 grammme of neutral red in 500 c. c. of alcohol and 500 c. c. water, also a solution of 13·61 grammes of mono-potassium phosphate ( $\text{KH}_2\text{PO}_4$ ), previously dried, in 1 litre of water, and  $\frac{1}{10}$  normal caustic potash solution. By mixing the phosphate solution and caustic potash solution in different proportions, standard solutions are formed with which the urine to be tested is compared, with the help of one or the other indicator. This colorimetric method, the details of which must be referred to in the original, is said to be simple and to furnish more reliable results than are obtained by the use of reagent papers.

### New Bornyval.

New Bornyval is the iso-valeryl-glycolic acid ester of borneol, having the chemical formula



Thus it contains 53 p. c. of borneol, 34·5 p. c. of valerianic acid and 25·7 p. c. of glycolic acid. It is a colourless liquid, almost without taste or odour; specific gravity 1·025—1·030,

boiling point 132° C. at 12 mm. pressure. It does not mix with water, but readily mixes with alcohol, ether, benzol and fatty oils\*).

Pharmacological and physiological tests of the preparation have shown that it is more resistant to acid liquids, such as gastric juice, than is bornyval (the iso-valerianic acid ester of borneol); it thus passes through the stomach unchanged and by the absorption of water in the intestine it is decomposed into its components (borneol, valerianic acid and glycolic acid). There is no difference in the pharmacological action of bornyval and new bornyval. New bornyval has the advantage over bornyval of possessing only a faint odour, so that the patients are not troubled by eructations. Preliminary experiments have shown that the ingestion while fasting of even 6 to 10 capsules of new bornyval gives rise to no troublesome symptoms in the stomach or bowels. A mild but not unpleasant sensation of warmth was noticed after taking the drug, but there was complete absence of unpleasant eructations and the appetite was not disturbed.

The indications for new bornyval are the same as those of bornyval\*\*). It is used both as a sedative and a nerve remedy in conditions of excitement of all kinds and as an analgesic in conditions of debility and collapse, in neuroses of the circulatory system, the digestive system and the central nervous system.

1 to 3 perles (0.25 grammes of new bornyval each) are given 2 to 4 times a day in milk, coffee or sugar and water.

### Ninhydrin.

The triketo-hydridene-hydrate, described in my last year's Report, is now put on the market under the name of ninhydrin. According to E. Abderhalden, it is used both as a test for albumin and also for the diagnosis of pregnancy. For this purpose, 2 to 3 c.c. of blood serum are poured on to 1 gramme of coagulated placental tissue in a diffusion capsule and the mixture is dialysed against 20 c.c. of water. This operation is allowed to proceed for 12 to 16 hours in

\*) Fortschritte der Medizin 1912, No. 46, p. 1471.

\*\*) Compare Merck's Reports 1903—1911.

Abderhalden, Münchener medizinische Wochenschrift 1912, No. 36, p. 1940. — Berliner tierärztliche Wochenschrift 1912, No. 36, p. 666.

the incubator at 37° C., the two liquids being kept covered meanwhile with toluol. 10 c. c. of the dialysate are mixed with 2 c. c. of a 1 p. c. aqueous solution of ninhydrin, the mixture is heated to boiling and kept at boiling point for exactly a minute. If the blood serum came from a pregnant woman, the reaction mixture turns blue, otherwise it remains colourless. In the same way proteolytic and peptolytic ferments can be demonstrated. In testing for carcinoma, carcinomatous tissue must be used in place of placental tissue, and in testing for tuberculosis, albumin obtained from tubercle bacilli must be employed. The blood serum used must be fresh and absolutely free from haemoglobin.

### Nitroglycerin.

As sea-sickness is a sign of anaemia of the central nervous system, O. Burwinkel tried the administration of nitroglycerin to sea-sick persons, giving from time to time, according to requirement, a tablespoonful of the following mixture:

Rp. Solut. alcoholic. nitroglycerini (1 p. c.) min. XX	Aq. destill. 150·0 grammes (5 oz)
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This medication brought about a rapid, though occasionally only a transient improvement. It may, if necessary, be repeated several times a day. Amyl nitrite gives rise to even greater cerebral hyperaemia than does nitroglycerin. The author therefore expects even better results from this drug. He has no personal experience of its use.

### Novaspirin.

Hagemann reports upon the employment of novaspirin\*) in biliary affections. He treated 5 cases, including a very severe case of gall stone disease, by means of 3 daily doses of 0·5 gramme ( $7\frac{1}{2}$  grains) of novaspirin, and always brought about the disappearance of the attack in the course of 2 to 3 days. The stools especially very rapidly assumed their normal colour. In a severe case of cholecystitis, in which the gall bladder was tightly stretched, the temperature was high, associated with vomiting, white stools and copious sweating, but in which there was neither jaundice nor bile

Burwinkel, Medizinische Klinik 1912, No. 29, p. 1199.

Hagemann, Therapie der Gegenwart 1912, No. 4, p. 192.

\*) Compare Merck's Reports 1906—1910.

pigment in the urine, the patient felt easier and more free from pain after two days' novaspirin medication. The temperature had also dropped. Novaspirin was equally efficacious in recurrences.

### Noviform.

Tetrabromo-pyrocatechin-bismuth is put on the market under this name. It is a yellow powder, without smell or taste, having the chemical composition  $\text{Bi}(\text{C}_6\text{Br}_4\text{O}_2)\text{OH}$ , and containing an amount of bismuth corresponding to about 32 p. c. of bismuth oxide. It is insoluble in water and only slightly soluble in organic solvents, such as alcohol and ether.

According to V. Borovansky, noviform can be sterilised without decomposition in a current of steam, it is not poisonous when administered internally and, on account of the bismuth contained, it has a desiccating action, limits secretion and promotes granulation formation; while the tetrabromo-pyrocatechin content endows it with antiseptic properties. It therefore answers all the requirements of a good dressing for wounds. The author has used the preparation in the form of gauze, pencils and ointments (10 to 20 p. c.) for venereal and surgical morbid tissue, for clean and infected cuts, furuncles, cellulitis, panaritium, paronychia, suppurating lymphoma, burns, varicose ulcers of the leg, also for plugging abscess cavities which have been evacuated and scraped out, for ulcers of the urethra and the anus and for the treatment of fistulas. The author also used noviform treatment for superficial forms of soft and hard chancres, open or opened ulcers, adenitis, periadenitis, broken down syphilitic ulcers, phagedenous soft sores and condylomata. It proved beneficial in every case and never gave rise to irritative symptoms or to other untoward secondary effects. The utility and absence of irritant effects of the new remedy were confirmed by E. Cammert, W. Michaelis, H. Million, Luksch and Most. According to L. v. Meyersbach, it may be spe-

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Borovansky, Medizinische Klinik 1912, No. 24, p. 992.

Cammert, Medizinische Klinik 1912, No. 47, p. 1912.

Michaelis, Berliner klinische Wochenschrift 1912, No. 41, p. 1940.

Million, Münchener medizinische Wochenschrift 1912, No. 34, p. 1852.

Luksch, Zentralblatt für die gesamte Therapie 1912, No. 8, p. 394.

Most, Zentralblatt für die gesamte Therapie 1912, No. 8, p. 393.

Meyersbach, Zentralblatt für Chirurgie 1912, No. 25, p. 841.

cially recommended for children who have a delicate skin and a tendency to eczema.

A. I. M. Lamers used noviform with satisfactory results after gynaecological operations. He states that the remedy is also useful in intertrigo, on account of its desiccating and disinfecting properties, in which it causes the rapid disappearance of the symptoms. In extreme obesity, copious discharge, prolapse, etc., and in vesico-vaginal fistulæ, it rapidly alleviated the subjective symptoms.

F. Dornheim discusses the value of noviform in otorhinology. The author used the preparation in complete mastoidectomies. He was able to confirm the properties possessed by noviform of limiting secretion and of bringing about desiccation in these cases. With regard to the development of granulations under the influence of this remedy, it is, according to Dornheim, kept within moderate limits, e. g., the preparation has neither a stimulating nor a corroding effect, which would abnormally promote or check the formation of granulations. As regards this characteristic it lies between the stimulating effect of iodoform and the corroding property of isoform. In combination with iodoform, and especially with isoform, used alternately, the author employed noviform with good results in the treatment of radical operations. The process of epidermis formation was always effected well and more rapidly, especially when in the last stage of treatment, the secretion having ceased, a mixture of noviform and scarlet red (4+1) was insufflated. Dornheim has also employed noviform as a plug after intra-nasal operations, particularly after resections of the septum, without observing any injurious effect. He even believes to have observed that noviform, like xeroform, possesses to some extent a haemostyptic action.

L. v. Liebermann jr. treated 25 cases of blepharitis with noviform in the form of 5 to 20 p. c. ointment (with vaseline). In ulcerative blepharitis this ointment may be spread on in a thin layer night and morning, after the scabs have been softened and removed. Existing conjunctivitis and follicular abscesses are treated separately. The ointment is also beneficial

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Lamers, Medizinische Klinik 1912, No. 45, p. 1832.

Dornheim, Deutsche medizinische Wochenschrift 1912, No. 50, p. 2367.

Liebermann, Deutsche medizinische Wochenschrift 1912, No. 11, p. 512.

in blepharitis in the presence of blepharo-conjunctivitis, if the scales are previously removed. In simple squamous blepharitis or seborrhœa sicca of the eye-lids, without demonstrable affection of the conjunctiva, the author obtained better results by the employment of noviform ointment than by the use of the customary remedies.

### Novocaine.

Experiments with mixed anaesthetics led A. Hoffmann and M. Kochmann to the conclusion that the combination of various local anaesthetics with potassium sulphate, which also possesses anaesthetic properties, increases the strength of the anaesthesia far above the arithmetical mean. While a concentration of at least 0·5 p. c. of novocaine had been proved in practice to be required for local anaesthesia, the authors found that after the addition of potassium sulphate to the injection fluid a 0·25 p. c. solution, or under certain conditions even a 0·1 p. c. or 0·05 p. c. solution of novocaine sufficed. But, in order to avoid failure, it is generally advisable to use a 0·1 p. c. solution as a substitute for the 0·5 p. c. novocaine solution of Braun. Its composition is as follows:

Rp. Novocaine	0·1 grammes ( $1\frac{1}{2}$ grains)
Sol. Potass. sulph. (2 p. c.)	20·0 grammes ( $\frac{2}{3}$ oz)
Sol. Sod. chlor. (0·9 p. c.)	ad 100·0     „     (3 $\frac{1}{3}$ oz)
Sol. Suprarenin. hydrochlor. (0·1%)	gtts. XII.

M. Sig.:  $\frac{1}{10}$  p. c. Novocaine-potassium-suprarenin solution.

Of this solution the authors injected 110 c. c. in an operation for carcinoma, 60 c. c. in an operation for haemorrhoids, 110 c. c. in an operation for splitting up of fistulas and resection of the scapula (osteomyelitis scapul.), 60 c. c. in an arthrotomy, 130 c. c. in an operation for carcinoma of the oesophagus, and so forth; the results were satisfactory in every case and in the majority of cases no after-pains occurred. The amount of anaesthetising fluid required was, according to the authors, not greater than that usually required for similar operations. The minute doses of potassium sulphate injected with the novocaine solution are practically negligible and are no disadvantage. On the other hand, on account of the comparatively small amount of novocaine required when given in conjunction

with potassium sulphate, other untoward secondary effects of novocaine, such as sickness, nausea and vomiting are eliminated. The authors have occasionally observed these after using the 0·5 p. c. novocaine solution of Braun. With few exceptions, novocaine-potassium-suprarenin solution did not give rise to pain after the anaesthetic effect had passed off.

The advantages of novocaine for inducing anaesthesia have been fully discussed by H. L. Baum. Reference may also be made to the communications of K. Siebert on some new methods of anaesthesia, in which, among other points, the successful results of sacral anaesthesia by means of novocaine-sodium bicarbonate solutions, originated by Läwen, and its technical performance are discussed.

### Nucleinic Acid.

Interest has recently been awakened in nucleinic acid therapy for the treatment of haemophilia after Sicard and Guttmann had achieved complete success in two cases of acquired haemophilia, which had lasted for 12 and 14 years. On account of its harmlessness further experiments might advantageously be carried out; though the diagnosis between haemophilia and purpura is occasionally attended with difficulty. The authors administered an intramuscular injection of 0·15 gramm (2 $\frac{1}{3}$  grains) of sodium nucleinate in 15 p. c. solution every 5 to 6 days, which resulted in a cure.

Nucleinic acid treatment is equally effectual in scarlet fever and erysipelas. M. G. Molia kow studied the action of the drug in 90 cases, and obtained good results, especially in the early stages of the disease. If the injections were given on the second day of the illness, all the symptoms rapidly subsided, while the temperature fell; if treatment were not commenced until the third to sixth day of the illness, the results were less striking. But in these cases also a favourable influence could be observed, while, compared with other methods of treatment, the mortality was reduced. For a dose, the author prescribed 0·1 gramm (1 $\frac{1}{2}$  grains) of sodium nu-

Baum, Deutsche medizinische Wochenschrift 1912, No. 51 and 52.  
Siebert, Medizinische Klinik 1912, No. 48.

Läwen, Merck's Report 1910, p. 256.

Sicard-Guttmann, Bulletin et mémoires de la société médicale des hôpitaux de Paris 1912, Vol. 28, p. 171.

Molia kow, Russkij Wratsch 1912, No. 9, p. 301; Semaine médicale 1912, p. 178.

cleinate for each year of life, so that a child aged ten would receive 1 grammie. This amount he considers the maximum dose, and he has never exceeded it. Continuous pain at the site of injection sometimes occurs for 1 to 2 days as a secondary effect. Besides this, the patients frequently suffer from headache. On the other hand, infiltration was never observed. Moliakow obtained a beneficial effect with the use of nucleinic acid injections in erysipelas and in acute articular rheumatism. In articular rheumatism he found that an injection of 1 grammie (15 grains) of sodium nucleinate brought about the cessation of pain. His experiments in typhoid, on the other hand, were not accompanied by marked success. He undertook these in the hope that the leucocytosis excited by the medicament might here also prove of use. The injection of nucleinic acid also led to negative results in several cases of dothienenteritis.

E. B. Blumenau has also expressed his views as to the value of sodium nucleinate in erysipelas. His communications are of special value, inasmuch as his experiments were carried out on 77 women who were suffering from a severe form of the disease, accompanied by marked toxic symptoms, irritation of the meninges, severe headache, pains over the whole body, vomiting and rapid pulse. Intramuscular injection (into the buttocks) is, according to the author, preferable to subcutaneous injection. The site of injection was disinfected with alcohol and ether, and after the injection with tincture of iodine, by which means complications were eliminated. At first only 1 grammie (17 min.) of a 10 p. c. solution was injected, and later a dose of 2 to 3 grammes (34 to 50 min.) in obstinate cases. The application was repeated every 2 or 3 days, and days were selected on which the fever varied, in order to exclude the possibility of the therapeutic effect coinciding with a natural improvement in the disease. The beneficial effect could be recognised by the fact that in about half the cases the crisis took place after a single injection. The best results may be expected when the nucleinic acid is employed early, i. e., about the second day of the disease. The method, however, fails in septic erysipelas.

As appears from the communications in my last Annual Report, the value of nucleinic acid in the treatment of pro-

gressive paralysis is not yet generally recognised. C. Tsiminakis has recently again brought nucleinic acid to the fore. From his results, he concludes that the administration of nucleinic acid should not be condemned, as some authors have done, but should rather be recommended; for, apart from treatment by tuberculin and by killed cultures of staphylococci and streptococci, no other treatment for the disease is known. Even though nucleinic acid is not capable of arresting the mental deterioration of the patient in every case, still the author's results show remissions and improvement in a number of cases, which places nucleinic acid treatment in a favourable light. The author commenced the treatment of his patients, who all gave a positive Wassermann reaction, by giving 3 injections of salvarsan, 0.3 gramm (5 grains) being injected at intervals of a week. Twenty days after the last injection, he started the treatment by nucleinic acid. Every patient was given 8 injections at intervals of a week, a freshly prepared solution of 2 grammes (30 grains) of sodium nucleinate and 2 grammes (30 grains) of sodium chloride in 100 grammes ( $3\frac{1}{3}$  oz) of sterile water being used each time. Local symptoms of irritation were observed in only one case.

In consideration of the antitoxic property of nucleinic acid and of its property of exciting leucocytosis, which have been observed by various authors, H. J. Achard used an aqueous solution of sodium nucleinate for treating wounds. He treated various wounds by first cleansing them with sterile water and then applying gauze compresses soaked in the above solution; or else he irrigated the wounds with the lotion and then applied an aseptic dressing. His results were satisfactory in every case.

The significance of nucleinic acid in therapeutics is also shown in a paper by M. Tschernoruzki "On the mutual action of nucleinic acid and nuclein-splitting ferment in the animal organism". He points out the far-reaching analogy of action exercised on the organism by nucleinic acid on the one hand, and infection on the other. Both occasion hyper-leucocytosis, rise in temperature, disturbance of the general health, increased metabolism; both exert an influence on fermentative

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Tsiminakis, Wiener klinische Wochenschrift 1912, No. 49, p. 1939.  
Achard, New York Medical Journal 1911, Vol. 94, No. 16, p. 779.  
Tschernoruzki, Biochemische Zeitschrift 1912, Vol. 44, No. 5 and 6.

processes and effect a certain degree of immunity. According to Tschernoruzki, this analogy undoubtedly shows that both nucleinic acid and infection act upon one and the same side of the animal organism, give rise to similar reactions and stimulate the same protective apparatus. According to this, we apparently possess in nucleinic acid a substance which exercises a stimulating action upon the natural protective power of the organism and more particularly upon the leucocytic apparatus. This shows the therapeutic significance of nucleinic acid and forms a basis for its therapeutic employment.

### Omnopon (Pantopon).

J. Kretschmer's experience tallies with Ewald's observation that in some cases of diabetes doses of 0·01 to 0·02 grammie ( $\frac{1}{6}$ — $\frac{1}{3}$  grain) of omnopon may prove efficacious in reducing the amount of urine, and to a slight degree the excretion of sugar also, this action is, however, transient.

E. Pasch reports a case of haemoptysis, in which he gave two subcutaneous doses of 0·02 grammie ( $\frac{1}{3}$  grain) of omnopon. There was a slight attack of perspiration, after which the haemorrhage ceased and the rapid pulse rate diminished. Omnopon produced equally good results on the recurrence of haemoptysis, morphine having failed. The author believes that haemoptysis furnishes a specially useful indication for omnopon.

J. J. Frankenstein tried the administration of omnopon in a case of opium habit. The patient was taking 15 grammes ( $\frac{1}{2}$  oz) of tincture of opium daily and, as a result of his continuous indulgence in opium for many years, he had become emaciated and degenerate. The author chose omnopon for treatment, because it is nearly related to opium in composition and can readily be given subcutaneously. He injected 1·1 c. c. a day of a 2 p. c. solution at first and gradually diminished the dose in the course of about 2 months, during which time the patient merely suffered from languor for a few days. The intestinal symptoms were insignificant. The treatment ended in complete success.

Kretschmer, Berliner klinische Wochenschrift 1912, No. 47, p. 2221.  
Pasch, Allgemeine medizinische Zentral-Zeitung 1912, No. 47, p. 614.  
Frankenstein, Medizinische Klinik 1912, No. 41, p. 1669.

According to J. Piket, omnopon is suitable for children; its influence on the respiratory centre is much slighter than that of morphine and its effect on pain and cough is greater than its styptic action. He prescribed the drug for cough, pertussis, enteritis, appendicitis, as an analgesic after operations and in a case of basal meningitis. It was not used for children under nine months of age. Older children were given on an average as many drops as they were years old of a solution consisting of 0·2 grammes (3 grains) of omnopon and 10 grammes (170 min.) of water or 12 grammes (200 min.) of *mistura gummosa*. A dose of 10 drops was, however, not exceeded, and as a rule only one dose was given a day. In every case this medication displayed a prompt action, the cough was rapidly checked, the night's rest was not disturbed and an improvement in the symptoms soon became manifest.

Jahrsdörfer records his experiences with omnopon in psychiatric practice. According to him, it has proved valuable, both by itself and in combination with scopolamine, when injected subcutaneously. In time a kind of habituation may occur, but symptoms due to abstinence are altogether wanting. Other secondary symptoms occasionally observed were insignificant.

E. Klausner and Rozabal, on the other hand, have described secondary symptoms of omnopon. After the subcutaneous injection of the drug, Klausner observed cutaneous phenomena in the form of erythema and nettle-rash, the severity and extent of which varied. The author refers these phenomena to chemical action and considers them to be drug rashes and not due to idiosyncrasy. After the injection of 0·02 grammes ( $\frac{1}{3}$  grain) of omnopon into a hysterical subject, Rozabal observed severe vomiting, loss of speech, miosis and headache; the symptoms disappeared in the course of 30 to 40 hours.

In the crises of tabes omnopon and morphine should, according to H. Winternitz, be employed with a certain amount of caution, though omnopon offers less danger of res-

Piket, *Klinisch-therapeutische Wochenschrift* 1912, No. 46, p. 1345.  
Jahrsdörfer, *Dissertation Heidelberg* 1912.

Klausner, *Münchener medizinische Wochenschrift* 1912, No. 40,  
p. 2170.

Rozabal, *Revista de medicina y cirujia practicas* 1912, p. 110.

Winternitz, *Therapeutische Monatshefte* 1912, No. 3, p. 169.

piratory disturbance than does morphine; the latter also very rarely gives rise to respiratory disturbance.

The communications of E. Popper, H. Winternitz, E. Stierlin and N. Schapiro on the action of omnopon on the digestive tract, and in relation with the action of opium, can only be referred to.

Omnopon has also been introduced into veterinary medicine. B. Meyer tried it with good results for the treatment of gastric and intestinal catarrh and for pharyngeal catarrh in dogs. According to the size of the dog, he injected 0·3 to 0·5 c. c. of a 2 p. c. solution of omnopon, which rapidly produced a sedative action.

### Orcin.

A. Jolles describes a method of testing for pentose, which depends upon the use of Bial's reagent, a solution of orcin in concentrated hydrochloric acid\*) and containing iron chloride. The process, which is of general interest, as by it pentose may be detected in the presence of glucose, is as follows:

The percentage of glucose is first established and then 100 c. c. of urine are taken for examination; in the presence of less than 5 p. c. of glucose 4 grammes of phenyl-hydrazine hydrochloride and 8 grammes of sodium acetate are added, and in the presence of 5 to 10 p. c. of glucose, double the amount of the two salts are added. This solution is heated for one hour on a water-bath and the osazone precipitate which results is transferred to a filter and allowed to drain thoroughly. The precipitate is transferred from the filter to a beaker, 15 c. c. of hot water are added, and the mixture is heated for 5 minutes on a water-bath and then filtered. The filtrate is submitted to distillation. For this purpose a flask

Popper, Deutsche medizinische Wochenschrift 1912, No. 7, p. 308.  
Winternitz, Münchener medizinische Wochenschrift 1912, No. 16,  
p. 853.

Stierlin - Schapiro, Münchener medizinische Wochenschrift 1912,  
No. 50, p. 2714.

Meyer, Berliner tierärztliche Wochenschrift 1912, No. 37, p. 683.  
Jolles, Zentralblatt für innere Medizin 1912, p. 693. — (Compare  
also ibid. 1907, p. 1049.)

\*) Compare Merck's Reagenzien-Verzeichnis 1908, p. 23 or Merck's  
Report 1903, p. 140.

of 400 c. c. capacity is used, having a discharge tube about 30 cm. in length fixed on to the neck and connected with a suitable glass condenser. 6 c. c. of hydrochloric acid (sp. gr. 1.19) are added to the filtrate and 6 c. c. are distilled over into a test-tube. 3 c. c. of the distillate are boiled for a short time with 5 c. c. of Bial's reagent. In the presence of only 0.05 p. c. of pentose the liquid assumes a distinct green colour.

Jolles has also elaborated a method by means of which saccharose may be demonstrated in the urine in the presence of other varieties of sugar\*). It depends upon the fact, previously found out by the author, that all kinds of sugar, with the exception of saccharose, lose their optic activity on being treated with caustic soda. To perform the test, urine which contains up to 5 p. c. of glucose is diluted with an equal amount of water, that containing over 5 p. c. of glucose with double the volume of water. Next, 2.5 c. c. of four times normal caustic soda are added to 100 c. c. of the mixture, which is heated continuously for 24 hours in a thermostat at 37° C. When cool, it is rendered slightly acid with acetic acid. 50 c. c. are made up to 55 c. c. with 10 p. c. lead acetate solution; it is shaken, filtered and polarised. A slight negative rotation excludes the presence of saccharose, while a positive rotation demonstrates the presence of saccharose, which can be estimated up to 0.2 p. c.

## Organotherapeutic Preparations.

### Adrenalin, Paraneprin and Suprarenin.

Specially gratifying results have been obtained by the use of adrenalin in bronchial asthma (nervous), in which, according to F. Gaisböck, the subcutaneous administration of 0.5 to 1 c. c. of the preparation has an almost specific effect. In the presence of acute danger, all other drugs having failed, intravenous application is indicated, which must be repeated until the effect remains permanent. At the same time cardiac tonics should be prescribed. It is well to combine these with the internal administration of morphine, scopolamine

\*) Biochemische Zeitschrift 1912, Vol. 43, p. 56. — (Compare Apotheker-Zeitung 1910, p. 1022.)

Gaisböck, Therapeutische Monatshefte 1912, p. 573.

and codeine. In one case of severe attacks of asthma the author injected adrenalin several times a day in combination with hyoscine hydrobromide (0.00015 grammes). The internal administration of the following solution also proved useful for continuous use: Extr. bellad. and Codein. phosph. aa 0.1 grammes ( $1\frac{1}{2}$  grains) in 100 grammes ( $3\frac{1}{3}$  oz) of aq. laurocer. Ten drops of this were given every half hour, and symptoms of intolerance never occurred. But after every fifth or sixth day injections of adrenalin were required. The injections were also beneficial in emphysema with severe attacks of breathlessness and stoppage of secretion.

Gaisböck also used adrenalin with benefit in chronic nephritis, and in acute nephritis with general oedema and oliguria, and in acute and subacute circulatory debility in infective diseases, when other excitants, such as strophanthin, digalen, theobromine, caffeine and camphor had proved ineffective. Contra-indications are severe cardiac disease and especially coronary sclerosis, endocarditis and aortalgia. Caution is also necessary in phlebitis, after haemorrhage and embolism have occurred, and in the presence of very high arterial pressure.

Besides the authors mentioned, Pisani, Fuchs and Roth, Blühdorn, Ephraim, Voigt, Rhode and Ogawa have expressed some very favourable opinions on the treatment of asthma, bronchitis, cardiac insufficiency, dyspnoea and dropsy.

Voigt considers adrenalin one of the most efficacious drugs in commencing disturbances of compensation and for bringing about increased diuresis in dyspnoea and dropsy. He gave 0.3 to 1 c. c. subcutaneously and intravenously, in some cases with striking results. In cardiac weakness following diphtheria, Blühdorn considers that the drug should only be given subcutaneously and in doses of 1 to 5 c. c. (beware of intravenous injection.)

In bronchial asthma and chronic bronchitis the action of adrenalin (suprarenin) depends upon the method of its em-

Pisani, Riforma medica 1912, No. 3.

Fuchs-Roth, Zeitschrift für experimentelle Pathologie und Therapie 1912, Vol. 10, p. 187.

Blühdorn, Münchener medizinische Wochenschrift 1912, No. 23.

Ephraim, Deutsche medizinische Wochenschrift 1912, No. 31.

Voigt, British Medical Journal 1912, I, p. 536.

Rhode-Ogawa, Archiv für experimentelle Pathologie 1912, Vol. 69, p. 202.

ployment. According to Ephraim, the effect is slightest when inhaled, much greater but transient when given subcutaneously, and greatest and most lasting after endobronchial application.

For the treatment of cardiac debility at the climacteric, A. Martin prescribed synthetic suprarenin hydrochloride. He gave 5 to 8 drops of the 1:1000 solution 1 to 3 times a day, according to the constitution of the patients. Patients who had undergone this medication for 1 to 4 months showed definite strengthening of the heart without any secondary affection of the stomach. All the patients noticed considerable diminution of their troubles, especially of fatigue, headache and insomnia. The effect, however, only lasted for a few hours, so that the medication had to be repeated. No cumulative action of suprarenin was observed.

A communication by Herzberg appears to me of interest in gynaecological practice. The author recommends for the treatment of leucorrhœa vaginal irrigation with a solution of zinc salt and alum, to every 100 c. c. of which he adds 1 to 2 c. c. of adrenalin (0.1 p. c.). In suitable dilution this combination is said to be very useful for various acute and subacute inflammatory conditions of the female urogenital tract.

For the preparation of an anaesthetising fluid, Hackenbruch employed a mixture of 100 c. c. of 0.5 or 1 p. c. solution of novocaine in normal saline solution with 50 drops of paranephrin. The author prefers paranephrin to synthetic suprarenin, because in his experience it has a better constricting action on the vessels.

Naamé obtained very good results in Asiatic cholera by the subcutaneous injection of 3 to 5 c. c. and the intravenous application of 2 to 3 c. c. of adrenalin.

Schlamp and Lichtenstern report upon the use of adrenalin in veterinary medicine for macular disease of horses. Schlamp, as the result of his large experience, re-

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Martin, Berliner klinische Wochenschrift 1912, No. 37, p. 1735.

Herzberg, Halbmonatsschrift für soziale Hygiene und praktische Medizin 1912, Vol. 20, No. 18, p. 336.

Hackenbruch, Zeitschrift für ärztliche Fortbildung 1912, No. 20, p. 637.

Naamé, Therapeutische Monatshefte 1912, p. 376.

Schlamp, Münchener tierärztliche Wochenschrift 1911, No. 15.

Lichtenstern, ibid. 1911, No. 18. — Berliner tierärztliche Wochenschrift 1912, No. 12, p. 211.

commends the subcutaneous injection of 2 to 4 c. c. of adrenalin, mixed with 10 c. c. of sterile water, for moderately severe and very severe cases. At his suggestion, Lichtenstern used adrenalin in two cases, but only one was cured. He also considers intramuscular application best and attaches importance to the use of fresh adrenalin solutions.

Reference may be made to the chemo-therapeutic experiments of H. Engel, which give insight into the action of adrenalin and substances of similar constitution in animals affected by tumours.

### Carotid Gland.

C. Frugoni has occupied himself with the question of the internal secretion of the carotid gland (Luschka) and its action. His investigations furnished no direct proof, but he is of opinion that this gland, which is considered rudimentary, possesses a secretion which may, in certain circumstances, be augmented. He used fresh glands taken from young calves and, having first ground them up with powdered glass, he extracted them with normal saline solution, using aseptic precautions. The fluid extract, with the addition of a little chloroform as a preservative, was standardised so that 4 c. c. corresponded to one gland.

4 to 6 c. c. of the carotid extract, injected intravenously into a rabbit weighing 1.5 to 2 kilogrammes, kill it within a minute. The symptoms of poisoning consist primarily in increased vascular tone, followed by a fall in the same, which is only interrupted again by a slight rise. Hereupon there is a rapid fall in blood pressure accompanied by paralysis of the lungs and ending in death. It is noteworthy that the heart continues to beat for a time. On dissecting the animal there is no evidence of either thrombi or haemorrhage, on the contrary, the blood is found to have lost its capacity for coagulation and even remains liquid for one or two days in vitro. The extract also gives rise to leucopenia. The fall in the blood pressure is not due to the alteration of the bulbar vasomotor centre, for if the central ends of the vagus and sciatic nerves be stimulated during the condition of low blood

Engel, Zeitschrift für experimentelle Pathologie und Therapie 1912,  
Vol. 11, p. 9.

Frugoni, Semaine médicale 1912, No. 41, p. 481.

pressure, the stimulation of the epigastric nerve causes an increase in the blood pressure, while that of the sciatic nerve causes its fall. Thus the extract appears to have a distinctly vasomotor effect and the fall of blood pressure is due to the vascular dilatation to which the extract gives rise. The extract has no debilitating effect upon cardiac activity. The repeated injection of small doses leads to a high degree of habituation, so that the experimental animal is finally able to tolerate 3 to 4 times the lethal dose without harm and without the occurrence of anatomical and pathological changes in the vessels. Finally the author offers experimental evidence to show that no reciprocal action of an opposite or inhibitive nature exists between the secretion of the carotid gland and adrenalin.

The results of Frugoni's investigations are for the present only of physiological and pharmacological interest. Carotid extract is not yet ready for therapeutic trial, apart from the fact that a suitable preparation of the organ has not yet been put on the market.

### Cerebrum.

I referred to the value of cerebral substance in nervous diseases some years ago in an article on organotherapy\*). Cerebrum siccatum, which is easily obtained, has generally been employed hitherto and has been given internally. Occasionally an emulsion has been prepared from fresh animal brain substance for subcutaneous injection; but this process is lengthy and inconvenient and not quite free from danger. Attempts have therefore recently been made to extract the cerebral substance by means of solvents, which can be sterilised and readily administered. Fontana reports upon his experiments with a preparation, so-called cephalopin, which is obtained by the extraction of cerebral substance by means of olive oil. He states that it has the advantage of not containing albumins or cytotoxins. It is said to contain the active principles of cerebral substance, with its detoxicating, antispasmodic and tonic effects. It is clear that in extracting the organ with a fatty oil, a large proportion of the lipoids pass into the extraction medium, but it has not yet been definitely proved

\* ) Compare Merck's Report 1908.

Fontana, Gazzetta degli ospedali e delle cliniche 1912, No. 48.

that these are the only active constituents of brain substance. But it may be assumed that an oily solution of this kind would have a beneficial effect in nervous affections, for the lipoids, especially lecithin, are recognised as valuable remedies in nervous diseases. The results obtained by Fontana with cephalopin in a number of cases, such as neurasthenia, hysteria and epilepsy are therefore not surprising, for similar results have frequently been obtained by the use of pure lecithin. It must be remembered that oily solutions are more slowly absorbed than are aqueous emulsions. Cephalopin is injected subcutaneously in doses of 1 to 5 c. c. As oily solutions are easily sterilised and keep well in ampoules, Fontana has not observed local symptoms of irritation after the application of the preparation.

### Corpora Lutea.

In view of the scarcity of publications on the therapeutic value of the corpora lutea\*) in gynæcological practice, reference may be made to the most recent communications by C. F. Burnam. The internal secretion of the corpus luteum and its relationship to the ovary, or to the ovarian secretion, as has been assumed by various observers, led the author to carry out organo-therapeutic experiments. He used an extract from the corpora lutea of swine, but intends to introduce those of other animals also, such as those of sheep and cows, into the field of his experimental work. He found that the internal administration of the preparation never gave rise to injurious by-effects and that it may be beneficial in cases of disturbed menstruation. This is more especially the case in amenorrhœa and dysmenorrhœa of young girls. Burnam attributes its action to various components of the corpus luteum, one of which is said to cause hyperæmia of the pelvic organs, while another must be regarded as a nerve stimulant. He further assumes the presence of a toxic substance, as he observed toxic symptoms after the intravenous application of the extract.

Kiutsi dissected out the yellow structure (lutein cells)

\*) Compare Merck's Report 1908, p. 10.

Burnam, Journal of the American Medical Association 1912, Vol. 59, p. 698.

Kiutsi, Monatsschrift für Geburtshilfe und Gynäkologie 1912, Vol. 36, p. 399.

from a fresh corpus luteum and carried out experiments with it, which showed that lutein extract rapidly coagulates women's blood. This suggests the idea that in normal ovulation the blood coagulation which takes place after the bursting of the Graafian follicle is brought about by lutein cells, the lutein substances penetrating into the blood and checking the menstrual flow.

W. Th. Sack carried out physiological investigations on the influence of corpus luteum on metabolism. He injected into rats an aqueous extract of corpus luteum and found that in female animals the percentage of nitrogen was considerably increased, while this was not the case in male animals. This excess of nitrogen is presumably made use of in some part of the female sexual apparatus. In order to clear up this question, he injected corpus luteum into female animals every second day and examined the organs in question at the end of a fortnight. He found that this treatment indeed effected a macroscopic change in the milk glands and the uterus and in the blood vessels supplying these regions.

J. L. Chiries' observations suggest the value of corpus luteum therapy in the vomiting of pregnancy\*). At the autopsy on a woman, who had died from persistent vomiting in the third month of pregnancy, he found that the corpus luteum was atrophied and in the act of regression. It was also much diminished in size by cyst formation and overgrowth of connective tissue. The author therefore believes the assumption justified that the corpus luteum was prevented through functional disturbance from fixing or rendering innocuous those poisons which had caused vomiting in the pregnant woman. This case supports the organotherapeutic employment of corpus luteum.

### Hormonal.

On further investigation\*\*) the value of hormonal has been found to be less than was anticipated.

Sack, Archiv für experimentelle Pathologie 1912, Vol. 70, p. 293.

\*) Compare Merck's Report 1908, p. 11.

Chiries, Gynäkologische Rundschau 1912, p. 707.

\*\*) Compare Merck's Reports 1910 and 1911.

L. Popielski attributes the action of hormonal to a vaso-dilator, which is present in all organs and which, on account of its property of reducing the blood pressure, has a secondary effect on peristalsis. On pharmacological investigation, hormonal showed no effect on the bowels when applied subcutaneously. A. Sabatowski arrived at the same conclusion. In man he also only obtained indefinite results after intramuscular administration. R. Dittler and R. Mohr sought to decide the question as to whether hormonal stimulates intestinal peristalsis by acting as a hormone, or whether Popielski's assumption is correct. They found that in animals even small doses caused a considerable fall of blood pressure and decreased the coagulability of the blood. After injecting hormonal into 13 cats, 3 rabbits and 1 dog, peristalsis only occurred in 4 cats and was arrested by the injection of adrenalin. The action of hormonal on resected pieces of bowel was quite negative. Thus the authors obtained no data of importance for the therapeutic employment of hormonal. W. Weiland, who carried out a pharmacological comparison between an intestinal extract and hormonal (prepared from spleen), came to the conclusion that the two preparations have a number of properties in common, but he was unable to decide whether the two preparations were identical. His intestinal substance, however, showed marked differences from vaso-dilatin-Popielski. No direct conclusions can be drawn from these statements.

The literature of the past year contained a somewhat animated discussion as to the value and the dangers of hormonal therapy. The contradictory opinions will be given as impartially as possible.

In chronic constipation, Pierret and Duhot injected hormonal intravenously in doses of 20 c.c. and obtained satisfactory results in 7 out of 9 cases. They state that the in-

Popielski, Münchener medizinische Wochenschrift 1912, No. 10, p. 534.

Sabatowski, Lwowski tygodnik lekarski 1912, Vol. 7, p. 31. — Compare R. Mohr, Wiener klinische Wochenschrift 1912, No. 20, p. 759.

Dittler-Mohr, Zeitschrift für klinische Medizin 1912, Vol. 75, p. 275. — Fortschritte der Medizin 1912, No. 31, p. 961.

Weiland, Archiv für die gesamte Physiologie 1912, Vol. 147, p. 171. Pierret-Duhot, Echo médical du Nord 1912, 28<sup>th</sup> July.

jection may be repeated when the action has passed off, e. g., after a few days.

Intravenous injection is in general preferred, especially in post-operative intestinal obstruction. W. Kausch reports a case of this description, in which the intravenous injection of 20 c. c. gave rise to flatus, and 23 hours later to choleraic diarrhoea. The author attributes the action to the hormone, while R. Mohr and A. Schönstadt believe it to be due to peritonitic irritation, and the latter author quotes a case in proof of this.

Groth employed hormonal in 14 cases of post-operative intestinal paralysis with only two failures. Quadrone and Glitsch were also well satisfied with the action of the drug.

Doubt has been thrown upon the assumed harmlessness of hormonal by a number of observations. Mohr, Schönstadt, J. Voigt, Birrenbach, G. Kleinberger, H. Boermann, R. Mühsam, W. Wolf, D. Frischberg, E. Rosenkranz, A. Hesse and J. Kretschmer observed serious symptoms of collapse after the intravenous or intramuscular application of the drug, and A. T. Jurasz met with a

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Kausch, Berliner klinische Wochenschrift 1912, No. 19, p. 881,  
No. 34, p. 1608.

Mohr, Berliner klinische Wochenschrift 1912, No. 26, p. 1225.  
Schönstadt, Berliner klinische Wochenschrift 1912, No. 48, p. 2277.

Groth, Medizinische Klinik 1912, No. 35, p. 1425.

Quadrone, Gazzetta degli ospedali e delle cliniche 1912, No. 125.

Glitsch, Archiv für Verdauungskrankheiten 1912, No. 4, p. 466.

Voigt, Therapeutische Monatshefte 1912, No. 10, p. 708, No. 11,  
p. 799.

Birrenbach, Münchener medizinische Wochenschrift 1912, No. 21,  
p. 1155.

Kleinberger, Münchener medizinische Wochenschrift 1912, No. 29,  
p. 1613.

Boermann, Münchener medizinische Wochenschrift 1912, No. 28,  
p. 1553.

Mühsam, Therapie der Gegenwart 1912, No. 7, p. 314.

Wolf, Münchener medizinische Wochenschrift 1912, No. 20, p. 1107.  
Frischberg, Münchener medizinische Wochenschrift 1912, No. 18,  
p. 990.

Rosenkranz, Münchener medizinische Wochenschrift 1912, No. 17,  
p. 931.

Hesse, Deutsche medizinische Wochenschrift 1912, No. 14, p. 643.

Kretschmer, Münchener medizinische Wochenschrift 1912, No. 9,  
p. 474.

Jurasz, Deutsche medizinische Wochenschrift 1912, No. 22, p. 1037.

fatal case after intravenous injection. All the authors attribute the unpleasant secondary effects to the preparation itself and not to its faulty administration. Zuelzer, also, states that hormonal displays secondary effects. But as some of the above named authors admit that the drug exercises a favourable influence on peristalsis and regard it a necessity to have a preparation which can be used intravenously or intramuscularly, hormonal could not be left altogether out of account. Zuelzer found on closer investigation that hormonal contained an albumose, which is thought to be responsible for the mishaps. On his advice, therefore, an albumose-free preparation has been made which is now put on the market exclusively for therapeutic purposes. The author has tried the new hormonal in a number of patients and has injected 20 to 40 c. c. intravenously without evident ill-effect.

### Hypophysis Preparations.

Very great interest was exhibited during the last year, especially by gynaecologists, in the new hypophysis preparations, pituitrin, pituglandol, glanduitrin and "vaporole" pituitary (infundibular) extract. These substances are essentially identical in composition and therapeutic action, for they are all prepared from the posterior lobe of the hypophysis, the so-called infundibular portion\*). But in employing the various special preparations the strength of the solution should be considered, for according to J. Hirsch, 1 c. c. of pituitrin contains the active principles of either 0.1 or 0.2 gramme of fresh hypophyses, and this is also the case for glanduitrin, while 1 c. c. of pituglandol corresponds to 0.1 gramme and 1 c. c. of "vaporole" pituitary extract to 0.2 gramme of hypophysis substance.

Nothing definite is at present known as to the chemical composition of the active principles contained in these preparations, but something may be gleaned from the communications of H. Fühner. The author found that in rabbits the intravenous application of pituitrin causes transient ces-

Zuelzer, Deutsche medizinische Wochenschrift 1912, No. 26, p. 1233.  
— Therapeutische Monatshefte 1912, No. 11, p. 798. — Münchener medizinische Wochenschrift 1912, No. 13, p. 706.

\*) Compare Merck's Report 1911, p. 336.

Hirsch, Therapeutische Monatshefte 1912, No. 11, p. 791.

Fühner, Münchener medizinische Wochenschrift 1912, No. 16, p. 852.

sation of respiration with a simultaneous rise in the blood pressure. The author carried out comparative tests with methylguanidin and histamin ( $\beta$ -imidazolyl-ethylamine), chemically pure substances with definite characteristics and equal action. He came to the conclusion that although histamin probably does not contain the active component of hypophysis extract, yet the active principle is pharmacologically nearly related to histamin, for it gives rise to the same symptoms on intravenous injection, and the respiratory and blood pressure curves correspond exactly to those observed after the employment of pituitrin. The author therefore recommends that until the active principle of the hypophysis has been chemically established and until it can be prepared in a chemically pure state, histamin should be used experimentally for clinical purposes in place of pituitrin, as exact dosage is possible in using this substance.

The following observers have tested hypophysis preparations in gynaecological cases:

E. Anderes, Korrespondenzblatt für Schweizer Ärzte 1912, No. 12, p. 454.  
V. Bagger-Jörgensen, Allmäna svenska läkartidning 1911, p. 818.  
W. Benthin, Therapie der Gegenwart 1912, No. 4, p. 156.  
Besserer, Deutsche medizinische Wochenschrift 1912, No. 28, p. 1358.  
H. Boermann, Münchener medizinische Wochenschrift 1912, No. 28, p. 1533.  
R. Cohn, Berliner klinische Wochenschrift 1912, No. 48, p. 2278.  
M. Eisenbach, Münchener medizinische Wochenschrift 1912, No. 45, p. 2445.  
R. v. Fellenberg, Korrespondenzblatt für Schweizer Ärzte 1911, No. 35.  
O. Fischer, Zentralblatt für Gynäkologie 1912, No. 1, p. 15.  
H. Fries, Deutsche medizinische Wochenschrift 1912, No. 37, p. 1730.  
Genter, Wratschebnaja Gazeta 1911, p. 1627.  
A. Ginewitsch, Russkij Wratsch 1912, No. 1, p. 18.  
Goebel, Münchener medizinische Wochenschrift 1912, No. 30, p. 1669.  
D. Grünbaum, Münchener medizinische Wochenschrift 1912, No. 38, p. 2048.  
W. Gussew, Zentralblatt für Gynäkologie 1912, No. 52, p. 1755.  
G. Hager, ibid. 1912, No. 10, p. 304.  
Th. Hagy, ibid. 1912, No. 10, p. 301.  
C. Hahl, Praktische Ergebnisse der Geburtshilfe und Gynäkologie 1912, Vol. 4, No. 2.  
A. Hamm, Münchener medizinische Wochenschrift 1912, No. 2, p. 77.  
H. Hansen, Ugeskrift for Laeger 1912, p. 257.  
K. Heil, Zentralblatt für Gynäkologie 1912, No. 42, p. 1398.  
S. Heilbronn, Münchener medizinische Wochenschrift 1912, No. 42, p. 2279.

A. Hengge, *ibid.* 1912, No. 51, p. 2814.  
O. v. Herff and L. Hell, *ibid.* 1912, No. 3, p. 132.  
J. Hirsch, *Therapeutische Monatshefte* 1912, No. 11, p. 790.  
J. Hofbauer, *Münchener medizinische Wochenschrift* 1912, No. 22, p. 1210.  
F. Jaeger, *ibid.* 1912, No. 6, p. 297.  
R. Th. Jaschke, *ibid.* 1912, No. 30, p. 1661.  
Kalefeld, *Deutsche medizinische Wochenschrift* 1912, No. 48, p. 2272.  
R. Klotz, *Münchener medizinische Wochenschrift* 1912, No. 38, p. 2047.  
L. Lagane, *Presse médicale* 1912, No. 59, p. 613.  
F. Lehmann, *Zentralblatt für Gynäkologie* 1912, No. 35, p. 1147  
W. Liepmann, *Therapeutische Monatshefte* 1912, No. 8, p. 569.  
le Maire, *Ugeskrift for Laeger* 1912, p. 251.  
M. Malinowsky, *Zentralblatt für Gynäkologie* 1912, No. 43, p. 1425.  
R. Marek, *Casopis lékaruv českých* 1912, No. 12.  
J. Melchior, *ibid.* 1912, No. 12.  
F. Merkel, *Münchener medizinische Wochenschrift* 1912, No. 35, p. 1933.  
J. Müller, *Berliner klinische Wochenschrift* 1912, No. 29, p. 1396.  
G. C. Nijhoff, *Nederlandsch Tijdschrift voor Geneeskunde* 1912, I, p. 806.  
R. Patek, *Zentralblatt für Gynäkologie* 1912, No. 33, p. 1083.  
Rieck, *Münchener medizinische Wochenschrift* 1912, No. 15, p. 816 and No. 52, p. 2872.  
R. Roemer, *ibid.* 1912, No. 38, p. 2046.  
P. Schäfer, *ibid.* 1912, No. 2, p. 75.  
Schirokow, *Russky Vratch* 1912, No. 26.  
Schlapoberski, *ibid.* 1912, No. 26.  
H. Schmid, *Deutsche medizinische Wochenschrift* 1912, No. 41, p. 1933.  
G. Trapl, *Monatsschrift für Geburtshilfe und Gynäkologie* 1912, No. 4, p. 393.  
J. Voigt, *Frauenarzt* 1912, p. 214.  
Voll, *Münchener medizinische Wochenschrift* 1912, No. 38, p. 2050.  
A. Weymersch, *Journal médical de Bruxelles* 1912, No. 16.

It appears that hypophysis extract has on the whole proved very useful for labour pains, if given by subcutaneous or intramuscular injection in doses of 0.5 to 1 c. c. once or, if necessary, several times. In the first and second stages it markedly abbreviates the duration of labour if no obstruction is present. According to Hofbauer, 7 c. c. may be given in the course of 24 hours without apprehension. In the first stage it is most effective when, in primipara the os is about  $\frac{4}{5}$  dilated, and in multipara when the os admits two fingers. In the absence of pains, its action, according to Jaeger, is of short duration. In the second stage the employment of the drug disposes of the use of forceps in many cases, while version and difficult breech extractions are no longer required. It is, therefore, in general indicated in primary and secondary

inertia, in ineffective pains due to extreme distension of the uterus by hydramnion or twins, in threatened displacement, placenta prævia and in contracted pelvis. Directly after the birth of the child, caution is necessary in injecting hypophysis before the placenta has come away, as it may prevent the expulsion of the placenta. After the placenta has been expelled, however, the hypophysis medication may be continued, if treatment is required for post-partum haemorrhage. It may then be combined with ergot. Hypophysis is equally useful in haemorrhage due to subinvolution of the uterus.

Injection of hypophysis is also useful as a prophylactic before the performance of Cæsarian section, as it reduces the haemorrhage. But it fails in attempts to bring on premature labour or abortion, and is not advisable in the latter. In the induction of premature labour, it is only useful when combined with rupture of the membranes. At the termination of normal labour the action of hypophysis appears to be doubtful; positive cases have been recorded, but in other cases it partially or entirely failed. At any rate it is only efficacious immediately before the natural commencement of pains.

Hypophysis injection may also be tried in post-partum atony. Liepmann reports a case in which the severe haemorrhage could not be checked by ergot, secacornin, rest in bed and application of an ice-bag, while one injection of 1.1 c.c. of pituglandol had the desired effect. Schmid likewise recommends the employment of hypophysis injections for the treatment of severe atony before resorting to extirpation of the uterus. He states that up to 6 c.c. may be injected into the uterine cavity without apprehension.

Injections of hypophysis are contra-indicated in those cases in which strong pains are undesirable and also in cardiac and renal diseases (Klotz-Malinowski). But the last-named contraindications are doubtful, for Hofbauer injected hypophysis without ill-effect in cases of goitre-heart and nephritis. It is still an open question whether the contra-indications should be extended to the earliest stages of the first period and to cases in which rigidity of the os is likely to occur; in any case caution should be exercised in these cases, for various authors have observed uterine spasm (strictures) (Patek, Hamm, Rieck, Heil, Voigt). Other secondary effects are also occasion-

ally met with after injections of hypophysis. J. Miller and D. Lewis have observed transient glycosuria after the injection into animals. Hengge observed the reduction of cardiac activity in both mother and child. This occurred in a case in which he had not combined the administration of hypophysis with simultaneous injection of morphine-scopolamine (dawning-sleep), according to his own suggestion. Really threatening symptoms did not occur, with the exception of a case reported by Bovermann, in which he met with severe, prolonged syncope after the combined administration of pituitrin and ergot for the treatment of haemorrhage following an abdominal operation. He therefore recommends caution in the employment of injections of hypophysis and ergot for patients who have lost much blood.

F. Fromme reports upon his experiments with injections of hypophysis in amenorrhœa. In a number of cases he injected 1 c. c. of pituglandol daily up to 10 days and succeeded in re-establishing the menses. In other cases this therapy partially or completely failed. Further experiments are required to show whether suitable cases can be diagnosed beforehand.

Krakauer injected 1 c. c. of pituglandol in a case of eclampsia at the sixth or seventh month of pregnancy in a nulliparous patient, with the result that premature labour occurred and the woman regained consciousness. On the strength of this case, the author considers hypophysis injections to be a valuable aid in the treatment of eclampsia.

R. Klotz attributes 3 effects to pituitrin, viz., it causes a fall in the blood pressure, brings about intestinal paralysis and increases diuresis. Its utility therefore comes into consideration in peritonitis. The author obtained good results by the injection of the preparation in two cases. He also expects to obtain good results from the use of hypophysis preparations on account of their stimulating action on peristalsis. In one case, which had proved exceedingly refractory to other remedies, he gave an intramuscular injection of 2 c. c. slowly in the course of 10 minutes, with a complete success.

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Miller-Lewis, Archives of Internal Medicine 1912, Vol. 9, p. 601.

Fromme, Zentralblatt für Gynäkologie 1912, No. 41, p. 1366.

Krakauer, Berliner klinische Wochenschrift 1912, No. 49, p. 2317.

Klotz, Münchener medizinische Wochenschrift 1912, No. 38, p. 2047.

According to C. Koch, hypophysis injections may prove beneficial in osteomalacia. He reports upon 3 cases. One severe case was cured by means of a daily injection of 2 c. c. of pituitrin and the total use of 190 c. c.; two milder cases were improved by the injection of 3 c. c. of pituglandol or 5 c. c. of pituitrin. The only secondary effects observed were pains at the back of the head at the commencement of the treatment.

O. Weiss used a combination of suprarenal extract and hypophysis extract, so-called asthmolysin, with benefit in asthma. This remedy is said to be more efficacious than suprarenal extract by itself. It is given by subcutaneous injection.

Finally, reference may be made to a communication by H. v. Willebrand. According to his experience, hypophysis injections may be beneficial in the circulatory disturbances of diphtheria.

A communication by R. Hoffmann deserves consideration; he states that the vital part of hypophysis is to be found not in the infundibular portion, but in the epithelial portion of the gland. As theoretical considerations of the relationship of hypophysis and cerebro-spinal fluid and of the entrance of hypophysis secretion into the latter make it appear probable that with deficient secretion of the gland and with the presence of too small an amount in the cerebro-spinal fluid, disturbances of metabolism may occur in the central nervous system, the lumbar application of the epithelial hypophysis colloid is not without therapeutic prospect. But as the extract obtained from a gland is never of the same value as its secretion, the author uses as a substitute the serum of thyroidectomised and ovariectomised sheep, because in this serum, after operation, the production of hypophysis colloid appears to be increased. According to Hoffmann, the blood pressure curve following the injection of this serum is indeed similar to that following the employment of pituitrin. A serum prepared by me at Hoffmann's suggestion is at the present time undergoing physiological examination.

Koch, Medizinische Klinik 1912, No. 25, p. 1022.

Weiss, Deutsche medizinische Wochenschrift 1912, No. 38, p. 1789.

Willebrand, Finska läkaresällskapets handlingar 1912, Vol. 54, p. 776.

Hoffmann, Zeitschrift für klinische Medizin 1912, Vol. 76, No. 5 and 6.

**Iodothyroin.**

L. Weil observed that in several women, after the administration of iodothyroin\*), pregnancy occurred, although these women in spite of having been married for many years had never conceived and were considered sterile. He therefore assumes that there is present in many sterile women a disturbance of the hormone reciprocal action of thyroid gland and ovary, and that this may be remedied by the administration of thyroid gland substance. The author obtained his results with iodothyroin; it has not yet been decided whether other thyroid gland substances, such as thyroidin, furnish equally good results. He prescribed at first one tablet a day of iodothyroin and increased the amount to 2 tablets 3 times a day. We must await the confirmation of the action of iodothyroin or of thyroidin in the direction described. In repeating Weil's experiments, it is, of course, essential to ascertain whether conception is excluded by any gynaecological cause and, if necessary, an examination must be made of the spermatic fluid of the husband.

**Mammin.**

Mamma therapy is particularly beneficial, as I reported some time ago\*\*) in a special article on organotherapeutic preparations, in menorrhagia, metrorrhagia, dysmenorrhœa and uterine fibroids. This has been confirmed by L. Adler, who carried out both therapeutical and pharmacological experiments with mamminum Poehl, an extract prepared from udders of cows. The pharmacological experiments on rabbits and guinea-pigs showed the effect of mammin injections on the suprarenals and on the uterus. The suprarenals increased considerably in weight, up to 3·5 times the normal weight, no doubt on account of hyperæmia of the cortex and of the medullary substance. The suprarenals also showed areas of inflammatory infiltration, which consisted of lymphocytes, leucocytes and especially of (lymphocytic) plasma cells. In other parts mitosis occurred. The author is unable to explain the significance of these phenomena.

Weil, Münchener medizinische Wochenschrift 1912, No. 42, p. 2283.

\*) Compare Merck's Report 1908, p. 38.

\*\*) Compare Merck's Report 1908, p. 70.

Adler, Monatsschrift für Geburtshilfe und Gynäkologie 1910, No. 1.

— Münchener medizinische Wochenschrift 1912, No. 1.

The effect of mammin injections on the uterus was evident by the early interruption of pregnancy and the expulsion of the ovum, without harm to the animals. The author therefore assumes that the mammary gland causes the normal expulsion of the ripe ovum by means of an internal secretion, acting by way of the suprarenal glands; thus, as the ovum by its growth gives rise to the enlargement of the mammary gland and perhaps also to an internal secretion running parallel with it, the foetus provides for its own expulsion by the action of the mammary gland. The author is continuing his investigations.

### Mesenteric Glands (*Cœliacin*).

Schwerdt some years ago pointed out the value of the mesenteric glands in scleroderma. W. Kölle tried this organo-therapeutic treatment in the same disease with very satisfactory results. The author prescribed for a woman, aged 37, 2 tablets a day of 0.3 gramme of dried mesenteric gland substance (so-called *cœliacin*), together with massage and hydro-therapeutic measures. The tablets were so well tolerated that he increased the dose to 3 tablets. In about 6 weeks the patient had gained about 4 pounds in weight, there was a striking improvement in her appearance, the vascular supply to the skin of the face was everywhere good, the glossiness had disappeared, it was much less tense and could be moved freely in all parts; the subcutaneous tissue had in almost all parts returned to its normal consistency, the skin of the face and brow could once more be wrinkled and the oedema of the thoracic wall had disappeared. Induration was still present in the thighs alone. The purely atrophic areas of the hands and feet had, however, remained unaltered. The patient could walk much better. The nights were less disturbed than before treatment. Subsequently, by further administration of the organic extract, the improvement was maintained in a surprising manner. Although the case has been under observation for much too short a time to allow a definite opinion to be formed, yet the result recorded by the author is so encouraging that this organo-therapeutic treatment deserves full consideration in similar cases. The author explains the effect

Schwerdt, Merck's Report 1908, p. 13.

Kölle, Münchener medizinische Wochenschrift 1912, No. 16, p. 864.

of the administration of mesenteric gland by supposing that it replaces the absent function of the mesenteric glands, e. g., the autotoxins are rendered innocuous. Kölle does not support the view that the autotoxins act directly on the organs supplied by the sympathetic, which are manifestly alone attacked in the morbid picture of scleroderma and the above explanation would perhaps in part account for improvements in the morbid symptoms. Nor, in his opinion, does the sympathetic undergo alteration; it may under certain circumstances regain its functional capacity, the organs which it supplies, provided they have not degenerated, may recover and it would be possible along these lines to imagine a complete cure.

### Ovaraden-Triferrin.

Lau reports upon his experiments with ovaraden and ovaraden-triferrin. Ovaraden, like other preparations of the ovary, comes into consideration when the function of the ovary is deficient. It must be given for a prolonged period to furnish a result. It is, therefore, administered in the form of tablets, 1 tablet being given after meals twice a day until 200 tablets have been consumed. If the result is insufficient, one or two further courses must be given. In the majority of cases, the troubles will thus be removed if the women have not been castrated. In the latter case the organotherapy treatment must be permanent, or must at any rate be continued until the organism has become accustomed to the artificial menopause.

As the majority of women affected by disturbances of the ovary usually suffer also from more or less severe chlorosis, Lau suggests the combination of organotherapy with the administration of iron preparations, or the administration of ovaraden-triferrin, which besides ovarian substance contains a well-tolerated iron preparation (triferrin)\*). As the result of his two years' experience of this drug in dysmenorrhœa and amenorrhœa, the author draws the conclusion that ovaraden-triferrin has a favourable influence upon the commencement of menstruation, the general health, loss of appetite, fatigue, sensation of distress, epistaxis, vaso-motor disturbances and lumbago. It is also beneficial in climacteric symptoms. Further,

it is indicated in the chlorosis of young girls, for chlorosis is now assumed to be connected with diminished ovarian activity.

Lau's experiences with ovaraden-triferrin have been confirmed by E. Otto and K. Hoffmann. Hoffmann prescribed the preparation, usually with benefit, for women who had to undergo operation for tumours of the ovaries and adnexa of both sides, and in whom the whole of the ovarian tissue, or the greater part of it, had to be removed. Women who, on account of the artificial menopause thus produced, suffered much from hot flushes, headache, etc., were usually beneficially affected by the drug. Even though failure is occasionally met with, yet, according to Hoffmann, the good results frequently obtained in cases in which there is no other means of treatment form ample compensation. J. Sonnenfeld arrived at similar conclusions; in the indications mentioned above, he combined the administration of ovaraden-triferrin with that of Dürkheimer Maxquelle.

### Ovaries.

M. Neu and A. Wolff, in carrying out an experimental study on the question of the myoma-heart, observed that the human ovary contains comparatively much iodine, viz., 0.46 milligramme in 1 gramme of fresh substance. This discovery is not without interest as regards the relationship between the internal secretion of the iodine-containing thyroid gland and the ovary, and not without importance for ovarian therapy itself\*). But B. Zoepritz, on repeating the experiments of the above named authors, was unable to confirm their results. Although he employed an approved and sensitive method, Zoepritz was unable to demonstrate the presence of iodine in the human ovary. Even when iodine or lipo-iodine was administered before the operation, no iodine could be demonstrated. This certainly shows that the ovaries do not possess the power of selectively taking up iodine.

Otto, *Der Frauenarzt* 1912, No. 10.

Hoffmann, *Reichsmedizinalanzeiger* 1912, No. 21.

Sonnenfeld, *Deutsche medizinische Wochenschrift* 1912, No. 50.

Neu-Wolff, *Münchener medizinische Wochenschrift* 1912, No. 2,  
p. 72.

\*) Compare Merck's Report 1908, p. 77.

Zoepritz, *Münchener medizinische Wochenschrift* 1912, No. 35,  
p. 1898.

G. Schickèle carried out investigations on the internal secretion of the ovaries. The author first found that the ovaries (uterus and menstrual blood) contain a substance which checks the coagulation of blood, and which constitutes an antithrombin of great efficacy. He also found the ovaries to contain a substance which lowers the blood pressure. The author considers these two substances to be hormones. But these are most probably not the only substances supplied by the ovary; other substances probably originate thence, e. g., those regulating the growth of bone, the development of the body in general, metabolism, etc.

### Placenta.

Placenta, according to the investigations of G. Schickèle, contains two physiologically active substances, which exert an influence on blood coagulation and on blood pressure. On employing the blood plasma of geese, he found it to contain a substance which hastens the coagulation of blood, and the injection of juice extract into rabbits effected the prolonged lowering of blood pressure. The depressor action of thyroid gland extract was increased by the simultaneous administration of placental extract, while the property possessed by adrenalin and pituitrin of effecting a rise in the blood pressure was neutralised. The property possessed by placental extract of effecting a fall in the blood pressure makes it appear probable that the placenta is capable of augmenting or of replacing the function of the ovaries and that it thus possesses an internal secretion. But the fact that the placenta contains a substance which lowers the blood pressure cannot be accepted in proof of this.

### Suprarenal Glands.

Th. Klein noted the effect of the internal administration of suprarenal gland in a case of Addison's disease. The case was a severe one, which rapidly grew worse in spite of all remedial measures, such as rest in bed, lying by an open window, suitable diet, tonics, iron and arsenic medication,

Schickèle, Biochemische Zeitschrift 1912, Vol. 38, p. 169 and 191.

Schickèle, Biochemische Zeitschrift 1912, Vol. 38, p. 214.

Klein, Deutsche medizinische Wochenschrift 1912, p. 1497.

so that the patient was finally unable to leave his bed on account of muscular weakness and could only move his limbs with difficulty. In this extremity, the author tried the administration of suprarenal glands\*), as had been suggested by various authors. He gave the patient, at first daily and later several times a week, two or three fresh, finely-minced suprarenal glands of sheep, together with other food or vegetables, or administered the juice pressed from the suprarenal glands.

This medication effected a striking, slow and steadily progressing improvement. The strength and weight increased, the pigmentation diminished, the gastro-intestinal troubles disappeared, the appetite and good digestion returned. The general strength improved to such a degree that the patient was able to go into the country and, with occasional repetition of the suprarenal medication, he felt exceedingly well. Only if the medication were discontinued for a prolonged period did the subjective and objective symptoms grow worse. From this observation the author draws the conclusion that the administration of suprarenal glands should always be tried in Addison's disease, for even though it did not effect a complete cure, yet it may prolong the life of the patients. Especially when other remedies have failed it should be tried, though it must be remembered that the prognosis is unfavourable even with the use of suprarenal preparations.

Sargent reports satisfactory results of suprarenal therapy in tuberculosis. He even obtained better results from the internal administration of suprarenal substance than from adrenalin. As the latter is contra-indicated in pulmonary haemorrhage, the internal administration of suprarenal gland may be recommended.

### Testiculin.

W. Karo reports upon his experiments with testiculin (glycerin extract of testicular substance 1:1) in the treatment of prostatic hypertrophy. The preparation was given by intra-gluteal injection at intervals of two days. An improvement in the morbid symptoms was manifest after each injection and

\*) Compare Merck's Report 1908, p. 15.

Sargent, Paris médical 1912, p. 247.

Karo, Dermatologische Wochenschrift 1912, No. 5, p. 139.

a cure resulted after 20 to 30 applications. The success of this organotherapy was absolutely definite in two cases which the author described in detail, for apart from testiculin no other medicament had been administered. The author describes a large number of cases in which this organotherapy proved beneficial. He therefore considers it justifiable and invites its further trial.

### Thymus Gland.

In Graves' disease, according to S. Solis-Cohen, operation should only be resorted to when the disease is too far advanced, or when a prolonged course of suitable treatment has proved unsuccessful. Besides rest, fresh air, nutritious food, correct diet, administration of much hot water before and between meals and sponging of the body, the author values organotherapy on the ground of his own experiences. He prefers thymus gland substance, of which he gives daily doses of 0.5 to 3 grammes ( $7\frac{1}{2}$ —45 grains) for months. He prescribes iodine ointments for local use.

Thymus preparation is well known to be beneficial in delayed development of children. C.G. Kerley and S.P. Beebe report upon this subject. To a boy, who in spite of his 16 years made the impression of an 11-year-old child, though he was not mentally backward, the authors at first prescribed rest, arsenic preparations and cod-liver oil for 9 months without obtaining any result, except an increase in weight. Only after a course of thymus did the boy grow in height and show sexual development. He received about 1 gramme (15 grains) of thymus extract a day.

### Thyrochrom.

Diesing's communication led G. Kelling to carry out experiments with thyrochrom tablets in cancer. He gave 2 tablets 3 times a day to a number of patients suffering from inoperable cancer, until a total of 200 to 600 tablets had been given. His case histories show that this medication was entirely without influence on the local symptoms of cancer.

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Solis-Cohen, American Journal of Medical Sciences 1912, Vol. 144, p. 13.

Kerley-Beebe, ibid. 1912, Vol. 144, p. 219.

Diesing, Merck's Report 1911, p. 341.

Kelling, Medizinische Klinik 1912, No. 16, p. 654.

The tablets never had an injurious effect and the author even gained the impression that they exerted a favourable influence upon the general health.

### Thyroid Glands (Thyroidin).

Years ago H. Stern pointed out\*) that the constituents of the human thyroid gland and those of the thyroid gland of the sheep generally used for medicinal purposes differ quantitatively. For example, the human gland contains 16 times as much arsenic as the sheep's gland. Although arsenic is not the sole active component of thyroid gland, yet the author believes it to be of great advantage in thyroidin therapy to combine the dried thyroid gland of sheep with two other substances, viz., arsenic and suprarenal substance. The composition of a single dose of the thyroid compound which he now uses is as follows:

Glandulæ thyroid. sicc.	0.05	gramme (3/4 grain)
Epinephrin	0.001	" (1/64 " )
Sod. cacodyl.	0.0005	" (1/125 " )

He chose sodium cacodylate because the preparation is very well tolerated and because it possesses a tonic action, which has a beneficial effect upon the cardiac debility usually present in a slight degree in most cases requiring thyroid gland treatment. He values epinephrin as a powerful analeptic, which not only has a favourable influence upon cardiac activity, but also serves as an antidote against certain thyroid gland toxins.

The author uses the above combination for falling out of the hair or alopecia, as he regards defective growth of hair as a symptom of hypothyroidism. The dose mentioned above is administered 3 times a day for a prolonged period, at least for 8 to 10 months. If it does not succeed, the falling out of the hair is due to some other cause. The cacodylate-thyroidin mixture has also proved useful in interstitial gingivitis, for which Stern gave 3 to 9 doses a day for 6 to 14 weeks. By means of this treatment 3 cases were completely cured and 7 were improved, while 4 cases remained uninfluenced.

Percy obtained good results by the use of thyroidin in chronic nephritis. The medication led to the disappearance

Stern, Berliner klinische Wochenschrift 1912, No. 48, p. 2253.

\*) American Medicine 1910, January. Compare Merck's Report 1910, p. 268.

Percy, Presse médicale 1912, No. 107, p. 1084.

of casts and albumin from the urine and to the regulation of the blood pressure, so that all subjective symptoms were removed.

W. J. Midelton assumes the presence of a certain degree of thyroid insufficiency in most cases of rheumatic arthritis; in cases showing myxoedematous symptoms, such as obesity, apathy, slow pulse etc., he administers thyroidin as well as the customary medicaments and excludes meat as far as possible. Too high doses must be avoided, wherefore the patient's blood pressure and pulse should be constantly watched.

Léopold-Lévi, who also connects migraine with functional disturbance of the thyroid gland, brings forward in proof of his assumption the fact that he succeeded in curing the symptoms of the disease, such as headache, by thyroidin medication. He believes that there are three varieties of thyroid gland migraine, one due to thyroid insufficiency, one to increased thyroid activity, and one between the two. The author administered 0.005 gramm (1/12 grain) of thyroidin 5 times a day, and for very definite insufficiency 0.02 gramm (1/3 grain). The dose may be reduced when improvement commences. During menstruation the drug is discontinued.

Thyroidin medication was further successfully employed by A. C. D. Firth in nocturnal enuresis, by R. Dupuy in infantilism, by R. Eager in mentally affected patients, by Minoret in constipation due to hypothyroidism, by Valmorin in eczema of infants, and by Variot in rickets\*).

The comparatively wide field of indication for thyroidin, which is shown in a large number of different symptoms, is a somewhat striking fact. It may be explained thus: the insufficiency of the thyroid gland and its defective secretion give rise to a large number of morbid symptoms, because the

Midelton, Practitioner 1912, Vol. 88, p. 180.

Léopold-Lévi, Bulletin de la société de thérapeutique 1912, p. 94.

Firth, Klinisch-therapeutische Wochenschrift 1912, No. 17, p. 519.

Dupuy, Revue de médecine 1912, Vol. 32, p. 307.

Eager, Journal of Mental Sciences 1912, Vol. 58, p. 424.

Minoret, Thèse de Paris 1911. — Klinisch-therapeutische Wochenschrift 1912, No. 17, p. 520.

Valmorin, Klinisch-therapeutische Wochenschrift 1912, No. 18, p. 547.

Variot, Bulletin de la société de pédiatrie (Paris) 1911, p. 208.

\*) Compare Merck's Report 1908, p. 36—55.

secretions of other organs have no opportunity of reciprocal action with the thyroid secretion. Another explanation is given by A. Siegmund, who assumes that the normal thyroid gland produces not only one but several active substances. Thus the thyroid insufficiency might be very varied if all these substances were produced in diminished amount, or if one or the other substance were produced in normal amount and the rest not at all. This assumption opens up a wide field for hypothesis. But it cannot be rejected off-hand, for Siegmund quotes examples from his practice, which show only too plainly that iodothyron, considered by various observers to be the active constituent of thyroid gland, cannot be the only active substance. He noticed that in the presence of certain morbid symptoms iodothyron failed when thyroidin was very effective, and vice versa. As the result of his observations, the author has not unjustly come to the conclusion that the thyroid gland produces many substances, the absence or abnormal structure of which explains the simultaneous occurrence of thyroid weakness and thyroid hypersecretion and their consequences. Each of the many substances probably has its special function and its special relationship with a definite tissue or organ, including other glands possessing internal secretions. If it remains absent or is only partially developed, a definite amount of harm ensues in a definite area of the organism. If several substances remain undeveloped, the morbid picture becomes more complex. It is evident from what has been said that thyroidin, consisting of dried animal thyroid gland, contains many substances, so that by its administration the diseased body may be supplied, not only with the deficient substance, but also with substances of which it already has sufficient or even too much. Thus, for example, palpitation and perspiration, to which thyroid treatment sometimes gives rise, must be regarded as a consequence of the introduction of too large a supply of one of the thyroid substances. But cases of this kind are rare.

According to Siegmund, the essence of thyroidin treatment lies not only in the supply of a substitute, but in the ability of the thyroid gland to rest and to collect new strength. "It is thus enabled to grow and gradually becomes capable of independent work." The author has repeatedly observed this

in children suffering from a benign form of thyroid weakness. The author finds further use for the administration of thyroidin in those cases in which other glands give forth an excess of secretion of a harmful nature, which can be neutralised by thyroid gland substances. In practice the following rules given by the author should be noted:

Very small doses of thyroidin are to be given to very young children. For mild cases in young babies daily doses of 0·05 grammie ( $\frac{3}{4}$  grain) suffice. Children of six often take 0·2 to 0·4 grammie (3—6 grains) very well. It is advisable to increase the dose carefully and to avoid meat diet as much as possible, as meat apparently contains substances poisonous to the thyroid gland.

In the treatment of every case it should be considered whether the patient is in need of preparations of other organs as well as of thyroidin; for mixed treatment is beneficial if the weakness of other glands occurs either as a cause, or produces concomitant symptoms, or is a consequence of weakness of the thyroid gland. The alternate administration of these preparations is often very advantageous. Special attention must be paid to the nose, for patients suffering from a benign form of thyroid gland weakness, especially of the myxoedematous type, are often affected by reflex neurosis of the nose, with symptoms in the head, trunk, limbs and female generative organs.

A treatise by W. Staehelin on the alteration of the normal blood picture in man after the administration of thyroid gland substance is of interest. The author found that under the influence of thyroidin medication the number of erythrocytes is not affected, while the white blood corpuscles are diminished in number. There is definite lymphocytosis and reduction of the neutrophile polynuclear leucocytes. The eosinophile leucocytes are sometimes increased in number, and sometimes their number remains unchanged.

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### Orgojod.

Orgojod is an iodised lecithalalbumin, which, according to Vorschulze, contains 20 p. c. of iodine. It is said to be

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Staehelin, Medizinische Klinik 1912, No. 24, p. 994.

Vorschulze, Fortschritte der Medizin 1912, No. 37, p. 1160.

an efficacious preparation, free from all the well known injurious properties of iodine. By the administration of 2 tablets 3 times a day the author obtained on the whole satisfactory results in several cases of syphilitic ulceration, pulmonary catarrh with exudative pleurisy, pulmonary distension with bronchial catarrh, stenocardia, gout, chronic articular rheumatism, bronchial asthma, scrofula and chronic bronchitis. In his opinion, the action of the drug is due to the iodine and lecithalalbumin which it contains; these stimulate the appetite and improve the nutrition. It has the advantage of not acting as an irritant upon the gastro-intestinal tract and upon the kidneys.

### Pancreatin.

L. Brieger drew attention to the action of pancreatin on carcinoma. His observations furnished two results. In some cases, both those in which operation had been performed and those which had not been operated upon, it was possible by the internal administration of pancreatin to reduce to normal the high antitryptic index, and sometimes even to reduce it permanently, with the result that the general health, the appetite and the weight were improved; but in other cases the antitryptic index was raised or it remained unaltered. A further study of these facts will perhaps admit of the use of pancreatin as a diagnostic and therapeutic agent in cancer and tuberculosis. The author first tried the action of pancreatin in combination with arsenic in pernicious anaemia. This, in his experience, is accompanied by a high antitryptic index of the blood. He was able to convince himself that the internal administration of pancreatin together with arsenic exerts a transient favourable influence.

The author prescribed as much as will go on the point of a knife of pancreatin to be taken 3 times a day before meals, and 2 drops of Fowler's solution, gradually increased to 8 drops, 3 times a day after meals. In 3 cases, which Brieger describes in detail, the medication brought about a strikingly rapid improvement. If arsenic were continued by itself, the deficiencies of pure arsenic therapy immediately became manifest, the improvement ceased, the threatening symptoms increased, while vomiting and diarrhoea occurred; these symp-

toms again disappeared on the administration of pancreatin. But the combined treatment was unable to effect a permanent cure, though in one case the antitryptic index was permanently rendered normal. It may, however, be assumed that by constant watching of the patients and by repeating the treatment described at definite intervals, the patients' lives may be prolonged.

In several patients suffering from cancer, Brieger was able by his method of treatment to effect a transient improvement with strengthening of the general condition, the carcinomatous process itself remaining uninfluenced.

### Paraffin, Liquid

In the treatment of wounds, liquid paraffin shows several good qualities, which encourage its employment in suitable cases. Auerbach, as the result of many years' experience, suggests the following method of use. Shortly before use, the paraffin is poured into a small sterile vessel. The author states that it is unnecessary to sterilise the preparation, as it possesses antiseptic properties and is chiefly used for suppurating wounds. After swabbing the wound and cleansing and drying the skin, the area surrounding the wound is painted with the preparation by means of a sterile swab of wool; cutaneous areas covered with hair are treated with special thoroughness. The wound and the area of skin to which paraffin has been applied are then covered with a dressing. This method of treatment is beneficial in two ways. It preserves the skin near the wound in a healthy condition, as it prevents irritation by secretion from the wound and thus eliminates the occurrence of itching and weeping eczema and of other disturbing processes; and it renders the change of dressing easier and more comfortable, as the dressing does not adhere so firmly. The paraffin does not protect against specific skin diseases, as for example eczema due to iodoform.

### Para-Nitro Diazobenzol Sulphate.

A dye consisting essentially of p-nitro-diazobenzol sulphate is put on the market under the name of "Azophor-red PN". It is obtained by evaporating to dryness diazotised p-nitraniline, to which aluminium sulphate has been added; it occurs as

a light brown powder, or light brown granules, which dissolve readily in water. If protected from light, the solution is said to keep for a long time without perceptible decomposition. The preparation is used technically as a red dye for cloth.

K. Feri suggests the use of azophor-red to simplify the diazo-reaction\*) for diagnostic purposes in the following way. A few granules of the preparation are shaken up with a little water and the solution is added to the urine to be tested, the latter having been rendered alkaline by means of caustic soda (not ammonia) until a slight turbidity has been produced. The reaction is only to be regarded as positive if the mixture assumes a bright red colour, and if on shaking the froth is also coloured red. The addition of acetic acid should only cause a slight alteration in colour.

According to Feri's investigations, this reaction has never failed when Ehrlich's diazo-reaction was positive, and it was always negative when the latter gave a negative result. The new modification of the diazo-reaction is said to be far more convenient and more easily performed; it is said not to require special knowledge or practice, and not to necessitate the employment of measured amounts of the reagents.

### Pergenol.

For the treatment of ulcerative forms of tuberculosis and syphilis of the larynx, Korte suggested a method in the application of which he used pergenol\*\*). By means of a suitable insufflator and with the help of a laryngeal mirror, a small quantity of pergenol in the form of powder is applied to the ulcer and this procedure is repeated 3 to 4 times in succession. The patient should try hard not to cough and should draw deep breaths. If he is then allowed to cough, much froth results and with it the whole of the mucus and dirty slough of the laryngeal ulcer is removed, leaving an excellent surface for caustic or corroding operations. Slight superficial erosions heal by themselves after the treatment described. Patients who work away from home can be treated with pergenol gargles and pergenol mouth pastilles as well. The author was

Feri, Wiener klinische Rundschau 1912, No. 24, p. 919.

\*) Compare Ehrlich's Diazo-reagent in Merck's Reagenzien-Verzeichnis 1913, p. 96.

Korte, Therapie der Gegenwart 1912, No. 1, p. 46.

\*\*) Compare Merck's Reports 1909 and 1910.

led to adopt this method on the assumption that by keeping the mucus disinfected by a greater or less supply of oxygen re-infection of the larynx might be prevented; the powdering was intended to prepare the way for any operative procedure which might be deemed necessary. The author has also found pergenol gargles and pergenol pastilles beneficial in the treatment of pharyngeal catarrh, bacterial inflammation of the throat, and tonsillitis. Pergenol, in the form of powder, also proved useful as a haemostatic in operations on the nose and throat, and as an application to the wound in tonsillectomies.

### Perhydrit.

Physicians have often expressed a wish to have perhydroxyl prepared in a solid form, suitable for use in practice. This desire cannot be altogether realised, because a solid preparation can only be formed by the combination of  $H_2O_2$  with other substances, and there can then no longer be any question of chemically pure hydrogen peroxide, such as is present in perhydroxyl\*). On the other hand, a solid preparation would undoubtedly be more useful for many cases and requirements in practice. I have therefore decided to introduce a preparation of this nature, which is put on the market under the name of "Perhydrit".

Perhydrit is a compound formed from perhydroxyl, consisting of hydrogen peroxide and carbamide (urea), which is rendered stable by a special process. It contains 34 to 35 p. c. of  $H_2O_2$ , and forms a white, crystalline powder, without odour, and remaining unchanged in dry air; it dissolves readily in water in the proportion 1 in 2·5, the hydrogen peroxide being split off. Solutions of perhydrit have a refreshing, salty taste. Apart from the carbamide they contain, they show all the characteristics and effects of corresponding solutions of hydrogen peroxide. The presence of carbamide does not prejudice the employment of perhydrit.

Although the solutions of perhydrit are not altogether equal in value to the chemically pure solutions of hydrogen peroxide prepared from perhydroxyl, yet they are quite useful in many cases. Perhydrit may be used in general practice,

\*) Although pure hydrogen peroxide can be prepared in a solid crystalline form, the characteristics of the preparation do not permit large quantities to be manufactured and put on the market.

when the carrying about of liquid perhydrol is inconvenient or impossible. The practitioner will often desire to have the solid preparation to hand, so as to be able to prepare a sufficiently strong solution of hydrogen peroxide by simple solution in water, be it for the careful removal of an adherent dressing, or in order to cleanse a very dirty or neglected wound. Perhydrit is well suited for carrying in the practitioner's instrument case. It may also be employed when a powder is required which will give off  $H_2O_2$ , by itself or in combination with other substances.

Perhydrit, especially in tablet form, is suitable for the preparation of solutions of hydrogen peroxide on journeys, e. g., for the preparation of a mouth wash or gargle. For the care of the mouth special perhydrit mouth wash tablets are put on the market. Perhydrit is also sold in substance and in 1 gramm (15 grains) tablets.

For the preparation of about 3 p. c. hydrogen peroxide solution, 1 part of perhydrit should be dissolved in 10 parts of water; for the preparation of about 1 p. c. solution, 1 part of perhydrit should be dissolved in about 30 parts of water. In order to hasten the solution of perhydrit, especially of the tablets, the water should be warmed to 35—40° C., particularly as Schmidt's investigations have shown that the disinfecting power of hydrogen peroxide is considerably greater at a higher temperature.

### Perhydrol.

In a communication on the pharmacodynamics of hydrogen peroxide, A. Nagy points out the great importance of acid-free hydrogen peroxide, as it exists in perhydrol. Its action comes chiefly into play when bacterial products cause the disintegration of tissue, and it furnishes mechanical support to the defensive efforts of the organism. It favours demarcation in inflammatory and gangrenous processes, both on the surface and in the deep parts of the diseased organs, and effects the elimination of injurious substances. Besides the mechanical action, the oxidising power of perhydrol comes into consideration in the complex chemical changes which

Schmidt, Zentralblatt für Bakteriologie 1910, Merck's Report 1910,  
p. 278.

Nagy, Allgemeine medizinische Zentral-Zeitung 1912, No. 35, p. 458.

occur in the disintegration of cells and tissues due to bacterial causes; through it the intermediate products of decomposition, which in part represent little differentiated substances, are rapidly oxidised and rendered innocuous. In these processes the presence of free acids may give rise to harmful by-effects and it is therefore justifiable to put forward as a condition that only an acid-free preparation be used for therapeutic purposes. Since the introduction of absolutely acid-free perhydrol into therapeutics, I have repeatedly drawn attention to this condition.

The work of N. Sieber on the hydrolysing power of perhydrol with regard to proteids, haemoglobin, haemin and tubercle bacilli at high temperatures and under a pressure of 3 to 6 atmospheres, and the resulting products can only be referred to here.

According to A. Ambroz, perhydrol is superior to a number of other hydrogen peroxide preparations as regards its disinfecting power, though this is in itself not of great consequence. The following bacteria, dried on silk threads, are killed by 2 p. c. perhydrol: anthrax bacilli in 5 minutes, typhoid bacilli in 10 minutes, bacillus coli in 10 minutes, and staphylococcus pyogenes aureus in 30 minutes.

Two papers by Ph. Fischer and Althoff, which deal with the customary method of employing hydrogen peroxide, are of interest. Whereas perhydrol contains 30 p. c. of  $H_2O_2$ , the solution of hydrogen peroxide of the German pharmacopoeia contains only 3 p. c.  $H_2O_2$ . But other preparations exist which contain  $H_2O_2$  in different proportions. It is always a matter of some difficulty for the dispensing chemist when he is required to make up a prescription of  $H_2O_2$  which has not been clearly defined. If, for example, a 10 p. c. solution of perhydrol is prescribed, there are two possibilities, either a mixture of 10 grammes of perhydrol with 90 grammes of water, which would correspond to 3 p. c.  $H_2O_2$ , or a mixture of 33 grammes of perhydrol with 37 grammes of water, which

Sieber, Zentralblatt für Bakteriologie I. Orig. 1912, Vol. 66, No. 7, p. 554. — Zeitschrift für physiologische Chemie 1912, Vol. 81, No. 1 and 2.

Ambroz, Zeitschrift für Hygiene 1912, Vol. 72, p. 470.

Fischer, Münchener medizinische Wochenschrift 1912, No. 20, p. 1108.

Althoff, Münchener medizinische Wochenschrift 1912, No. 26, p. 1438.

would correspond to 10 p. c.  $H_2O_2$ . In the same way it may be difficult to decide what the physician requires when he prescribes a 2 p. c. solution of hydrogen peroxide, a mixture of 2 parts of the official liquor hydrogenii peroxidi with 98 grammes of water, or a mixture of two parts of official liquor hydrogenii peroxidi with 1 part of water, the mixture in the first case containing 0·06 and in the second case 2 p. c.  $H_2O_2$ . The repeated complaints about these prescriptions call for the introduction of suitable rules. There are only two ways of clearing this point. Fischer suggests that in the prescription the percentage of  $H_2O_2$  should be given. Thus, if the physician requires a solution containing 3 p. c.  $H_2O_2$ , he can prescribe it as follows:

Rp. Hydrogen peroxide solution 3 p. c., prepared from perhydrol  
or

Rp. Hydrogenii peroxidi officinale.

The prescription leaves no doubt that in both cases a mixture containing 3 p. c.  $H_2O_2$  is required. In the first case the chemist will supply a mixture of 10 grammes of perhydrol and 90 grammes of water and in the second case the undiluted official preparation. Althoff prefers the more medical form of prescription. He would prescribe, for example:

Rp. Perhydrol	2·0—3·0
Aq. dest.	ad 300·0
M. Sig.: Gargle.	

Rp. Liq. Hydrogen. peroxid.	20·0—30·0
Aq. dest.	ad 300·0
M. Sig.: Gargle.	

Both suggestions are practically identical. Calculation is required by the chemist in one case and by the physician in the other. But in practice one of these suggestions should certainly be followed.

Several communications by J. Dodal, S. Stephenson, A. Weil and Eschweiler are of therapeutic interest.

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Dodal, Wiener medizinische Wochenschrift 1912, No. 9.

Stephenson, Lancet 1912, 16<sup>th</sup> November.

Weil, Journal de physiothérapie 1912, 15<sup>th</sup> March. — Revue de thérapeutique 1912, p. 20.

Eschweiler, Medizinische Klinik 1912, No. 33, p. 1343.

Dodal used perhydrol in a severe case of burning. The burns extended over a third part of the body and in consequence of the inept assistance of unqualified people and of the opening up of the blisters, infection was apprehended. As the presence of menstruation rendered the water-bath impracticable, the author irrigated the wound with 6 p. c. H<sub>2</sub>O<sub>2</sub> (20 grammes of perhydrol and 80 grammes of water). This procedure was repeated every 48 hours, when the ointment dressing was renewed. Although on the second day the wounds appeared to be suppurating and the patient was troubled with hiccough, eructations, etc., yet she was saved. On the sixth day, e. g., the third time the dressings were changed, the superficial wounds were clean and showed satisfactory granulations, and the more severely burnt areas were throwing off the necrotic skin without any particular inflammatory reaction. The perhydrol irrigations were completely painless and so efficacious that skin grafting was not required.

Weil recommends for the cutaneous pigmentations which occur as secondary effects of radiotherapy, and which may attack both physician and patient, after washing with soap and water (sodium peroxide soap), the application of the following ointment at night:

Rp. Perhydrol	5.0	grammes (90 min.)
Zinc. oxidi	5.0	„ (75 grains)
Lanolin.	20.0	„ ( $\frac{2}{3}$ oz)
Vaselin.	10.0	„ ( $\frac{1}{3}$ oz)

This treatment usually brings about the disappearance of the symptoms in a very short time.

Eschweiler declares a 1 p. c. solution of hydrogen peroxide to be extremely useful in otitis following scarlet fever. To avoid error (compare above), the author suggests the following prescription:

Rp. Perhydrol (Merck)	3.5	grammes (60 min.)
Aq. destill.	ad 100.0	„ ( $3\frac{1}{3}$ oz)

M. Sig.: For instillation into the ear.

As a solution of this kind will not keep long without the addition of a preservative, only small quantities should be prescribed. The ear is first syringed out and dried and the solution is then poured in without having been warmed. There is an immediate formation of froth, which comes bubbling out of the auditory canal. The liquid is left in the ear for

about 10 minutes and a Priessnitz dressing is then applied to the ear, with boric acid solution or aluminium acetate. The treatment and change of dressing must be carried out twice a day until the swellings of the auditory canal, the tympanic membrane and the cavity of the ear subside and the secretion is diminished. When the secretion has become reduced and the foetor has entirely disappeared, dry treatment may be resorted to.

In blennorrhœa neonatorum, Stephenson, before using silver nitrate solution, instilled perhydrol either undiluted or diluted with an equal amount of boiled water, with excellent results. The preparation decomposes and washes away the pus and the silver treatment is then more effective.

Perhydrol is superior to all other preparations as a disinfectant and deodoriser in the care of the mouth and the teeth. But here, as in so many other cases, it cannot be replaced by the acid official hydrogen peroxide, to which G. Ulkan draws special attention. After several applications of even weak solutions (0.5 p. c.) of the ordinary hydrogen peroxide in children, the author observed within 48 hours severe corrosions, the interdental papillæ being particularly severely affected, their apices sometimes becoming necrotic. Perhydrol mouth wash (Krewel), on the other hand, has proved of great value. The author has obtained nothing but good results by its use in gingivitis and stomatitis of children. After the regular use of the remedy acute inflammations of the mucous membranes subsided or improved in a short time.

Ulkan recommends the employment of perhydrol mouth wash in epidemics of diphtheria and scarlet fever among school children. Rinsing out of the mouth every time the children return home from school reduces the danger of infection and renders carriers of bacilli harmless. Gaertner also considers the disinfection of the mouth of carriers by solution of hydrogen peroxide to be the most satisfactory method of guarding against the danger of infection.

For bleaching the teeth, Brubacher recommends per-

Ulkan, Deutsche zahnärztliche Wochenschrift, Vol. 15, No. 48.

Gaertner, Münchener medizinische Wochenschrift 1912, No. 16, p. 899.

Brubacher, Deutsche zahnärztliche Wochenschrift 1912, Vol. 15, No. 51.

hydrol in combination with antiformin\*), this combination of both gives rise to the brisk development of oxygen. The author obtained very satisfactory results by cleansing discoloured teeth alternately with the drugs mentioned above and then rinsing the mouth with water and alcohol.

W. Sommer and Löffler report upon the employment of hydrogen peroxide in veterinary practice. Sommer prescribed "Hydrogenium peroxidatum medicinale purum 15 p. c." prepared by me, which is far superior to the ordinary official solution of hydrogen peroxide as regards concentration, purity and stability and which may be used in place of perhydrol, which is too expensive for veterinary purposes, although the former is less pure than the latter. According to him, it has proved highly serviceable in wounds due to stepping on nails, various wounds, chronic conjunctivitis, etc. As a rule, 1 to 3 p. c. solutions, freshly made from the preparation mentioned, are sufficient. Löffler also obtained very satisfactory results in the treatment of wounds by using the preparation in suitable dilution.

According to Peiser, perhydrol may prove of service in children's hospitals as a preservative for the milk of wet-nurses. Two drops of perhydrol and 0.2 grammes (3 grains) of calcium peroxide are added to 200 c. c. ( $6\frac{2}{3}$  oz) of milk, which is allowed to stand for half an hour in a Soxhlet at a temperature of 50° C. By catalytic action oxygen is liberated and prevents the decomposition of the milk. Perhydrol is added every second day and if amphoteric reaction of the milk occurs, more calcium peroxide is added. The author has had very good results with milk of wet-nurses preserved in this way.

Perhydrol has also been variously used for analytical and clinico-diagnostic purposes. P. Jannasch uses a mixture of pure concentrated (65 p. c.) nitric acid with 15 to 20 p. c.  $H_2O_2$  solution, prepared from perhydrol, for the destruction of organic matter in forensic analyses. By means of this mixture the sulphides formed by the precipitation of the metals belonging to the sulphuretted hydrogen group can be oxidised, without risking the formation of a disturbing brown coloration

\*) Compare Merck's Report 1908—1910.

Sommer, Berliner tierärztliche Wochenschrift 1912, No. 34.

Löffler, Zeitschrift für Veterinärkunde 1912, No. 7.

Peiser, Berliner klinische Wochenschrift 1912, No. 25, p. 1207.

Jannasch, Berichte der chemischen Gesellschaft Berlin 1912, p. 605.

on the evaporation of the solution thus obtained, which contains a large amount of sulphuric acid.

P. Melikow describes a sensitive reaction for molybdenic acid, for which he used perhydrol. The solution to be tested is evaporated to dryness on a water-bath, a slight excess of ammonia is added and 3 to 4 p. c. perhydrol. In the presence of molybdenic acid, a more or less intense red coloration results (with the formation of permolybdate). On again evaporating and adding sulphuric acid, the mixture is coloured yellow (with the formation of permolybdenic acid).

J. Boas describes a method, by means of which, in the investigation of the faeces for blood, as in the determination of gastric and intestinal haemorrhage, the presence of exogenous blood may be excluded. For this purpose the meat given to the patient is previously treated with  $H_2O_2$  to destroy the haemoglobin. This method is specially indicated when there is occasion to search for occult gastro-intestinal haemorrhage and when the first test for blood after partaking of meat or fish has been found to be positive. In this case, the gastro-intestinal canal is cleansed by means of a suitable aperient (magnesium sulphate) and the meat given during the next few days is treated with hydrogen peroxide, after which the faeces are again tested for blood. The haemoglobin is destroyed in the following manner: 100 to 125 grammes of scraped or minced veal or chicken are well mixed with 100 grammes of 3 p. c.  $H_2O_2$  in a porcelain dish. Much frothing results and the meat becomes white in colour. It is placed on a fine hair sieve and washed under the tap for 5 to 10 minutes, so that all superfluous  $H_2O_2$  is removed. The meat is served in the form of croquettes.

### Phenocoll Hydrochloride.

Phenocoll (amidoacet-p-phenetidin) was introduced into therapeutics in 1891 by R. v. Mering and Hertel, and according to Hertel, Herzog, Aronsohn, B. Balzer,

Melikow, Journal der russischen physikalisch-chemischen Gesellschaft 1912, Vol. 44, p. 608.

Boas, Deutsche medizinische Wochenschrift 1912, No. 44, p. 2060.

Hertel-Mering, Deutsche medizinische Wochenschrift 1891, No. 15.

Herzog, Merck's Bericht 1891, p. 56.

Aronsohn, Deutsche medizinische Wochenschrift 1891, No. 47.

Balzer, Dissertation Zurich 1892.

Kucharzewski, P. Cohnheim and others, it has proved a good antipyretic and antirheumatic. It is, according to Martinez Vargas, less useful as an antineuritic, though in pertussis it exerted a sedative action. This discovery of the last named author has recently found corroboration in the communications of J. C. Maleras, who used it successfully in an epidemic. To a large number of children (the majority under 11 years of age) he gave phenocoll hydrochloride in aqueous mixtures, with the addition of a suitable dose of heroin. Children were given 0.8 to 1.0 gramm (12—15 grains), and adults 2.0 to 3.0 grammes (30—45 grains) of phenocoll a day. Under the influence of this medication the coughing attacks were very quickly reduced in number and severity, so that after a fortnight's treatment 70 p. c. of the patients could be regarded as cured.

### Phenolsulphonephthalein.

The tests of the renal function elaborated by Geraghty and Rowntree by the use of phenolsulphonephthalein have been further investigated with a view to their usefulness by Montague, L. Boyd, Gardner, E. Sehrt, F. Deutsch, F. Fromme and C. Rubner, J. Vogel, W. Autenrieth and A. Funk and Goldberg. Vogel comes to the conclusion that phenolsulphonephthalein will shortly occupy an important position as a diagnostic of renal function on account of its rapid and complete excretion by the kidneys, on account

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Kucharzewski, Petersburger medizinische Wochenschrift 1894, No. 35.  
Cohnheim, Therapeutische Monatshefte 1892, No. 1.  
Vargas, Therapeutische Wochenschrift 1896, No. 1.  
Maleras, Medicina de los niños 1911, No. 12.  
Geraghty-Rowntree, Merck's Report 1911, p. 352. — Journal of the American Medical Association 1912, Vol. 60, p. 191.  
Boyd, Journal of the American Medical Association 1912, Vol. 58, p. 620.  
Gardner, Répertoire de pharmacie 1912, No. 7, p. 314.  
Sehrt, Zentralblatt für Chirurgie 1912, No. 33, p. 1121.  
Deutsch, Wiener klinische Wochenschrift 1912, No. 32.  
Fromme-Rubner, Berliner klinische Wochenschrift 1912, No. 40, p. 1889.  
Vogel, Berliner klinische Wochenschrift 1912, No. 46, p. 2172.  
Autenrieth - Funk, Münchener medizinische Wochenschrift 1912, No. 49 and 50.  
Goldberg, Münchener medizinische Wochenschrift 1912, No. 52, p. 2898.

of its great reliability and of the possibility in the majority of cases of readily and rapidly estimating the amount excreted by colorimetric methods and of thus being able to determine the functional capacity of the kidneys. Deutsch also confirms the usefulness of the preparation. He finds that within the first half hour measurable amounts are obtained, that these increase up to the end of the first hour, the height of excretion, and terminate after two hours. At the end of this time at least half of the injected phenolsulphonephthalein has been excreted. A deviation from this rule denotes pathological changes.

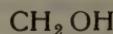
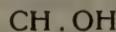
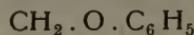
Autenrieth and Funk found that a kidney, which excreted less than 45 p. c. of the phenolsulphonephthalein in the first hour after intramuscular injection and less than 70 p. c. in the first two hours, has its functional capacity more or less disturbed. They therefore also corroborate the statements of Geraghty and Rountree. The same applies to Boyd, Sehrt and Gardner. Goldberg, on the other hand, found that the excretion of the dye varied so much, even in normal subjects and healthy kidneys, that he doubts whether the method is capable of replacing the inconvenient methods of investigation used hitherto. Fromme and Rubner obtained similar results after subcutaneous and intramuscular application of phenolsulphonephthalein; but on the ground of their experiments, they recommend intravenous injection, which they find less liable to error than the other methods. They also demand that the time of observation be extended to 3 hours, when at least 60 p. c. of the injected preparation should be excreted.

Although the authors mentioned have not all expressed an equally favourable opinion on the phenolsulphonephthalein method, yet it deserves further investigation; for when sources of error have been eliminated, it may be possible to construct a satisfactory method, or at least to elucidate the contradictory evidence of the various observers.

### **Phenoxypropandiol.**

A physiological and therapeutical study of this long known preparation has been published by M. Gardey. The author names the drug intended for therapeutic purposes *Antodynè*.

Antodyne is monophenol-glycerin ether, or glycerin-mono-phenyl ether, having the chemical formula



It forms fine, white needles melting at 69—70° C.; it dissolves readily in water, alcohol and other organic solvents, with the exception of petroleum ether. Its preparation and properties have been described by Th. v. Lindemann, Hantsch, Vock and Zivkovic.

By means of pharmacological experiments Gardey was able to prove that phenoxypropadiol is not poisonous to protoplasm. When used locally it has a weak anaesthetising action, and on the brain it appears to exert a powerful general anaesthetising effect. No influence has been detected on the blood and its composition, but in too large doses it diminishes the cardiac contractions and may lead to the death of the experimental animal with lowering of the blood pressure. In therapeutic doses the drug is said to be non-toxic.

From his experiments on animals the author concludes that phenoxypropadiol, in opposition to the view of Filippi and Rodolico, possesses no marked diuretic property, but it does act as a sedative, as was proved by experiments on human beings. Gardey states that by the use of the drug he has obtained a not inconsiderable analgesic action. In attacks of migraine doses of 0.5 to 1 gramme ( $7\frac{1}{2}$ —15 grains) sufficed to effect the desired result; in painful neuralgia, herpes zoster, tabes and gonorrhœal rheumatism daily doses of 2 grammes (30 grains) were required. The antispasmodic action was only tested in a case of chorea and gave a negative result. Nor has phenoxypropadiol any influence on the temperature of phthisical subjects, when given in therapeutic doses (up to 4 grammes [60 grains] a day). Thus the preparation at present only comes into consideration as an analgesic. According to Gardey, it may be administered in the form of powder or in

Lindemann, Berichte der deutschen chemischen Gesellschaft Berlin 1891, Vol. 24, p. 2145.

Hantsch-Vock, ibid. 1903, Vol. 36, p. 2064.

Zivkovic, Wiener Monatshefte für Chemie 1908, Vol. 29, p. 952.

solution in single doses of 0·5 gramm (7<sup>1</sup>/<sub>2</sub> grains), and daily doses of 1 to 4 grammes (15—60 grains).

### Phenylenediamine.

Meta-phenylenediamine, or its sulphate, is used by J. A. Siemssen as a test for gold salts, as he finds it very sensitive. The reagent consists of a solution in water 1:200, which if slightly coloured should be decolorised by animal charcoal. A solution containing only 0·005 gramm of gold chloride in 100 c. c. is coloured violet by the reagent. In the author's opinion, this colour reaction may be due to the separation of colloid gold (but it may with equal probability be caused by the oxidation of m-phenylenediamine).

Para-phenylenediamine is used to distinguish boiled and unboiled milk, according to Storch\*). A convenient modification of Storch's test is suggested by J. Tillmans. A mixture of equal parts of p-phenylenediamine (or its hydrochloride) with sea-sand on the one hand, and with barium peroxide on the other hand, is used. Both reagents are kept in suitable sprinklers and a pinch is shaken out into 10 to 20 c. c. of milk. First the p-phenylenediamine is added to the milk, and then the barium peroxide. Unboiled milk, after being shaken, is in a few seconds coloured dark blue over green. The blue colour can still be recognised if 2 p. c. of fresh milk has been added to the boiled milk. The subsequent addition of p-phenylenediamine usually augments the intensity of the colour, while excess of barium hydroxide produces a red coloration, as the solution assumes an alkaline reaction.

### Phosphotungstic Acid.

For the estimation of the albumin contained in gastric juice, which is useful in the diagnosis of gastric achylia, W. Wolff and P. Junghans use the following reagent:

Rp. Phosphotungstic acid	0·3 gramm
Hydrochloric acid	1·0     "
Alcohol (96 p. c.)	20·0 grammes
Distilled water	ad 200·0     "

Siemssen, Chemiker-Zeitung 1912, No. 98, p. 943.

\*) Merck's Reagenzien-Verzeichnis 1908, p. 249.

Tillmans, Zeitschrift für Untersuchung von Nahrungs- und Genußmitteln 1912, Vol. 24, p. 61.

Wolff-Junghans, Berliner klinische Wochenschrift 1911, No. 22, p. 978.

In order to carry out the test, different dilutions of the filtered gastric juice (drawn off after an Ewald test breakfast) are prepared, by making up 1 grammie, 0·5 grammie, 0·25 grammie, 0·1 grammie, 0·05 grammie and 0·025 grammie respectively of gastric juice to 10 grammes with water. These mixtures are poured into different test-tubes, and 1 c.c. of the reagent mentioned above is carefully added to each, so as to form a layer on the top. In the presence of albumin, a white ring appears at the junction of the two fluids. The amount of albumin is estimated by the degree of dilution of the first test-tube which proves too dilute for the formation of the ring, i. e., 10, 20, 40, 100, 200 and 400. K. Thiele carried out tests according to this method, and found that it might be most useful in the diagnosis of cancer, as an adjunct to other methods of diagnosis. It is distinguished by great simplicity and by the rapidity with which it can be carried out. The author diagnoses albumin values under 60 as benign achylia, those of 200—400 as carcinoma, and boundary cases of 100 rather as carcinoma than as benign achylia.

A further use for phosphotungstic acid is in urine analysis, in order to render the urine clear for the polarimetric examination of glucose. According to C. E. May, 50 c. c. of the urine to be tested are placed in a measuring glass of 150 c. c. capacity, acidified with a few drops of hydrochloric acid, 50 c. c. of a 2 p. c. solution of phosphotungstic acid are added, and the mixture is made up to 150 c. c. with water. After filtration, 100 c. c. are neutralised with barium hydroxide solution, made up to the mark with water and filtered. A solution prepared in this way is said to give good results in polarisation work.

O. Folin and W. Denis also use phosphotungstic acid as a test for uric acid, in a similar way to that suggested by Rosenberg 20 years ago. The reagent should be prepared by heating 100 grammie of sodium tungstate with 80 c. c. of phosphoric acid (85 p. c.) and 750 c. c. of water for two hours under a reflux condenser, and when cool, diluting to 1 litre with water. In order to carry out the test, an

Thiele, Berliner klinische Wochenschrift 1912, No. 12, p. 544.

May, Journal of Biological Chemistry 1912, p. 81.

Folin-Denis, Journal of Biological Chemistry 1912, p. 239 and 245.

— Zentralblatt für die gesamte innere Medizin 1912, Vol. 3, p. 231.

alkaline fluid is required. The author uses a saturated, aqueous solution of sodium carbonate. If 2 c. c. of uric acid solution are mixed with 2 c. c. of the reagent and 5 to 10 c. c. of sodium carbonate solution, the mixture becomes blue. Of course, the reaction has more than one interpretation, as the blue colour may be produced by other reducing substances.

The authors mentioned above suggest the following reagent in testing for phenols and for the colorimetric estimation of tyrosin in albuminous substances: 100 grammes of sodium tungstate and 20 grammes of phosphomolybdenic acid are heated with 50 c. c. of phosphoric acid and 750 c. c. of water for 2 hours under a reflux condenser. The mixture is allowed to cool and made up to 1 litre with water. Phenols in alkaline solution give a blue colour with the reagent. For the estimation of tyrosin, a fluid is prepared for comparison by dissolving 0.001 gramme of tyrosin in 5 c. c. of the reagent and 25 c. c. of sodium carbonate solution. Then 1 gramme of the albuminous substance to be tested is heated with 25 c. c. of concentrated hydrochloric acid for 12 hours, and the product of the reaction is made up to 100 c. c. with water; 2 c. c. of this are added to 5 c. c. of the reagent and 25 c. c. of sodium carbonate solution. The blue colour which results is compared with that of the comparison fluid.

### Physostigmine.

In tachycardia, R. Kaufmann carried out experiments with physostigmine which led to noteworthy results. He commenced with doses of 0.0005 gramme ( $1/125$  grain) of physostigmine salicylate and gradually increased the dose to 0.0015 gramme ( $1/40$  grain), a day and in exceptional cases up to 0.003 gramme ( $1/20$  grain). He usually combined this medication with the administration of digitalis and strophanthus. By this means he obtained prompt results in two cases of reflex tachycardia, and in 3 cases of essential, atrioventricular tachycardia. The attacks were in part cut short, and in part their recurrence was prevented. No positive result or only a very slight one was obtained by the treatment of a case of auricular tachycardia, and of a patient whose tachycardia was apparently due to ventricular fibrillation, and in tachycardia

accompanied by permanent arrhythmia. The author seeks the action of physostigmine in stimulation of the vagus, because its chief effect is seen in atrioventricular tachycardia.

### Picric Acid.

In my last Annual Report, I mentioned a communication by Schamberg and Kolmer, according to which picric acid solution is useful for preventing inflammatory symptoms of vaccination pustules. Schamberg has continued his researches and has been able to confirm his good results in a very large number of cases. In treating the pustules of 16 500 persons by his method, the author did not observe a single serious complication. The solution suggested by Schamberg consists of 4 grammes of picric acid, 1 gramme of iodine and 100 grammes of alcohol (95 p. c.). The arm is painted with this lotion 48 hours after vaccination has been performed, and the application is repeated at least once during the succeeding days. The process has the following advantages: The solution is capable of rendering the epithelial covering of the vaccination vesicle firm. On account of the components, picric acid, iodine and alcohol, which are all valuable anti-septics, the solution effects a diminution in the bacterial flora of the skin in the immediate neighbourhood of the vaccination vesicles, while it has a beneficial effect on the itching and the sensitiveness of the vaccination area. In many cases the vaccination lesion appears to run a more rapid course, and a hard crust is formed early.

L. Ortin recommends aqueous solutions of picric acid for loss of substance of the cornea and conjunctiva, and especially in ulcerative blepharitis. In acute and subacute conjunctivitis, it is no better than 2 p. c. solutions of zinc.

### Pilocarpine.

To promote the excretion of poison in veterinary medicine, especially in tetanus, a diaphoretic is frequently used, and for this purpose pilocarpine nitrate is most commonly employed. Very good results were obtained with it by Rémond and

Schamberg-Kolmer, Lancet 1911, p. 1397, 18<sup>th</sup> November.

Schamberg, Dermatologische Wochenschrift 1912, No. 44, p. 1355.

Ortin, Archivio de Oftalmologia, Barcelona 1912, July. — Wochenschrift für Therapie und Hygiene des Auges 1912, p. 71.

Aouizératé in two cases of acute tetanus in horses. They injected 0·1 gramme ( $1\frac{1}{2}$  grains) of pilocarpine nitrate into the animals 3 times a day for 4 or 8 days and succeeded in eliminating all morbid symptoms.

### Pinosol.

Pinosol is a new preparation of tar, which is distilled from tar under diminished pressure and is free from the toxic substances of ordinary tar. It represents a brown to brownish-yellow liquid, of the consistency of honey, which dissolves in chloroform, ether, benzol, petroleum and alcohol. It is insoluble in water and dilute alcohol, but forms an emulsion with them on the addition of alkalies. The skin is stained a faint yellow by treatment with pinosol, and can readily be cleansed by means of soap or soda. Pinosol does not irritate the skin, but renders it supple, so that it may even be applied to the face for cosmetic purposes. It has the property of dissolving iodine and sulphur and therefore facilitates the combined use of tar with these two important substances in dermatology\*).

J. Allert has treated 26 cases of skin diseases with pinosol, viz., psoriasis, chronic eczema, eczema marginatum, prurigo, pruritus senilis, herpes tonsurans, lichen ruber and seborrhœa capillitii, and obtained satisfactory results in every case. He never met with troublesome, toxic secondary effects, not even after prolonged administration to children. The preparation was used either pure or in the form of ointment (up to 20 p. c.). For children 5 p. c. ointments are sufficiently strong and may be rubbed in daily. For children under 5, affected by extensive areas of prurigo, Allert only applied the 5 p. c. ointment on alternate days and in the intervals applied inert ointments. Pinosol may be prescribed in the following forms: Rp. Pinosoli 10·0, Vaselini et Lanolini aa 45·0. — Rp. Pinosoli 5·0, Potassii carbon. 2·0, Ung. Glycerini 43·0. — Rp. Pinosoli 20·0, Sapo. mollis 30·0, Vaselini 50·0. — Rp. Pinosoli 5·0, Traumaticini 45·0. — Rp. Pinosoli 10·0, Zinci

Rémond-Aouizératé, Bulletin de la société de médecine vétérinaire 1912, 30<sup>th</sup> June. — Berliner tierärztliche Wochenschrift 1912, p. 778.

\*) Compare Pharmazeutische Post 1912, No. 93, p. 985.  
Allert, Österreichische Ärzte-Zeitung 1912, No. 18, p. 296.

oxid. et Amyli aa 25·0, Vaseline flavi 100·0. — Rp. Pinosoli 10·0, Sulph. depur. et Sapon. mollis aa 20·0, Past. Lassari 40·0. — Rp. Pinosoli 20·0, Aether. et Spirit. aa 75·0. — Rp. Pinosoli 5·0, Benzol. 10·0, Aceton. 35·0. — Rp. Pinosoli 2·0, Ol. Ricini 5·0, Spirit. 93·0. — Rp. Pinosoli 5·0, Zinci oxid. et Talc. aa 25·0, Glycerini 10·0, Aq. destill. ad 100·0. — Rp. Pinosoli 2·0, Zinci oxid. et Amyli aa 20·0, Glycerini 25·0, Aq. Plumbi 50·0. For mild cases of seborrhœa of the scalp, a solution of pinosol in bay rum may be used.

### Pittylen.

Acting on the experience that tar is useful for keratoplastic purposes and for the alleviation of itching, Herzberg prescribed pittylen in the form of soap for pruritus vulvæ. In the evening, before retiring to rest, the patient was given a warm sitz-bath, to which 2 tablespoonfuls of liquid, 10 p. c. pittylen soap had been added. Then 5 p. c. pittylen-menthol soap was rubbed to a lather on the affected areas of skin. The lather was allowed to dry and was sprinkled with zinc powder. On the following day it was washed with lukewarm water. If reddened, itching areas were present higher up the vagina, the author applied a 5 to 10 p. c. pittylen ointment after suitable vaginal irrigation. In every case the troublesome symptoms disappeared almost completely in a few days.

### Polygonum Hydropiper.

*Polygonum Hydropiper* is a member of the Polygonaceæ and is fairly widely distributed in Europe and America. It has been used as a remedy for jaundice, as a diuretic and an antirheumatic and in a similar manner to *Polygonum aviculare*, the so-called Homeriana tea. Apart from tannin, no substance was found in the plant which could be regarded as the therapeutically active agent. The hæmostatic action of the plant is certainly due to the tannin; it has recently been studied in detail by N. Krawkoff. But the author rejects the assumption that the hæmostatic power of the drug is due to tannic acid, as he could obtain no action by the use of the isolated tannins. He rather believes the

Herzberg, Medizinische Klinik 1912, No. 46, p. 1870.  
Krawkoff, Russky Vratch 1912, No. 7.

effect of the drug to be due to an alteration in the viscosity or in the coagulability of the blood.

Krawkoff used for his experiments a fluid extract prepared from the leaves of *Polygonum Hydropiper*; of this he prescribed 30 to 40 drops 3 times a day. In various forms of haemorrhage, as for example in haemoptysis, menorrhagia, gastric, vesical and haemorrhoidal haemorrhages, and in haemorrhages due to fibromyomata, it is said to have proved a valuable styptic, and in dysmenorrhoea an analgesic as well. It never gave rise to troublesome secondary effects and was always willingly taken.

### Polylactol.

The experience of various authors, such as Weiss and Lévai, that somatose (a pure albumose) is capable of increasing the secretion of milk, led to the production of polylactol, a preparation consisting of iron somatose, maltose and lactose. Iron somatose was chosen to provide a substitute for the deficient iron in mother and child in special cases, as for example in anaemia of the mother. The mother's milk is said to be made richer in iron by the administration of this iron preparation.

Netzer carried out experiments with somatose on goats and found that the quality of the milk is improved by this drug and that it is increased in amount, without giving rise to diarrhoea. This justified experiments on human beings. W. R. Hoeber found that polylactol is capable of checking the failing secretion of milk, thus allowing suckling to be continued. The author brings forward, as a proof of the true influencing of lactation by the drug, the fact that in the cases in which it had furnished a positive result, the discontinuation of the drug caused the secretion of milk to diminish or to cease.

A heaped teaspoonful of polylactol is prescribed 2 to 4 times a day in a little water, stirred up in milk, malt-coffee or beer.

Weiss-Lévai, Wiener medizinische Zeitung 1908, No. 41.

Netzer, Dissertation Giessen 1911. — Zentralblatt für die gesamte Therapie 1912, p. 559.

Hoeber, Allgemeine medizinische Zentral-Zeitung 1912, No. 35, p. 457.

### Potassium Hexatantalate.

After the results of Morgenroth's and Rosenthal's investigations had shown that potassium hexatantalate arrested the trypanocidal action of tartar emetic (potassium antimonyl tartrate), it was thought possible that potassium hexatantalate might be capable of transforming tartar emetic into a substance which was non-toxic or only slightly toxic to the entire organism. The pharmacological and chemical experiments carried out by Rosenthal and Severin indeed furnished the proof that tantalum treatment may render valuable service in stomachic antimony poisoning. Previously tannic acid had been used as an antidote for antimony poisoning; it renders the soluble antimony salts insoluble. But this action only took place if the poison had not entered the circulation.

The experiments were carried out on mice, which were given an absolutely lethal dose of tartar emetic by mouth. After a definite interval they received in the same way a suspension of potassium hexatantalate in normal saline solution. A suitable amount of tantalum salt entirely abolished the toxic effect; indeed a large proportion of the animals could be saved when the antidote was given an hour after poisoning. Less is to be expected from the parenteral application of potassium hexatantalate, even though a not inconsiderable number of cases of fatal antimony poisoning can be saved by its subcutaneous application.

The action of potassium hexatantalate is certainly due to the formation of an antimony-tantalum compound, which can also be obtained as a crystalline precipitate on the addition of tartar emetic to a solution of potassium hexatantalate.

### Propæsin.

R. Lüders and v. Boltenstern report upon the employment of propæsin (p-amido-benzoic acid propyl ester). Internally the drug is of value in vomiting in consequence of gastritis, acute gastric catarrh, gastric ulcer and carcinoma,

Morgenroth-Rosenthal, Merck's Report 1911, p. 362.

Rosenthal-Severin, Archiv für experimentelle Pathologie 1912, Vol. 68, p. 275.

Lüders, Klinisch-therapeutische Wochenschrift 1912, No. 23, p. 680.  
Boltenstern, Deutsche Ärzte-Zeitung 1912, No. 17, p. 264.

and in abdominal pain and sea-sickness. It is administered in single doses of 0·5 grammes ( $7\frac{1}{2}$  grains) (in cachets) and in daily doses of 4 grammes (60 grains).

In rhino-laryngology it may be used in all cases of injury to the mucous membrane of the larynx or mouth, in the form of insufflations for laryngeal tuberculosis, pertussis, affections of the tonsils and ulceration of the palate, and also in angina and chronic laryngitis. Propæsin mixed with milk sugar is useful as a snuff in nasal discharge, coryza of hay fever, and ulceration of the nose.

In dermatology, propæsin is useful in the form of a 15 p. c. ointment as an analgesic in ulcer of the leg, in pruritus of various origin, and in haemorrhoids.

In dentistry, propæsin is used for the treatment of pain after operations; it is applied to the alveoli or to the wound which has previously been cleansed. To prevent vomiting in dental operations, it may with advantage be sprinkled on the corresponding areas of the tongue and the palate.

In general, according to Lüders, free nerve-endings form the principal indication for the application of the insoluble anaesthetics, of which propæsin is one. They may also be employed in addition to the soluble anaesthetics (cocaine hydrochloride) to prolong the action of the latter\*).

### Prophylacticum Mallebrein.

Under this name a new remedy for tuberculosis has been put on the market. It consists, according to Mallebrein and Wasmer, of a 25 p. c. solution of aluminium chlorate,  $\text{Al}(\text{ClO}_3)_3$ , and when brought into contact with the secretions of the mucous membranes, the authors state that aluminium albuminate and free chloric acid are formed. The aluminium albuminate forms a deposit on the mucous membrane, where new firm particles of albumin are separated off, and this counteracts possible inflammatory softening. The chloric acid which is set free is further decomposed, and by its oxidising action brings about disinfection, in the same way as is effected by potassium chlorate. There need be no apprehension of aluminium chlorate giving rise to injurious action, as this was never observed.

\*) Compare Merck's Reports 1908 and 1909.

Mallebrein-Wasmer, Zeitschrift für Tuberkulose 1912, Vol. 18, p. 225.  
— Münchener medizinische Wochenschrift 1912, No. 12, p. 655.

According to Jarosch, aluminium chloride has proved of value in affections of the respiratory passages, especially in angina, and in other diseases of an infective nature, as for example in affections of the female genital organs.

In tuberculous affections of the lung, the patient is told to gargle 3 times a day with a mixture of 25 to 30 drops of prophylacticum Mallebrein and 3 tablespoonfuls of water, and to inhale an equal number of times a mixture of half the above strength. Special attention should be paid to the correct employment of the drug, as success will not follow its superficial and irregular use. Anyone who is unable to gargle or finds difficulty in inhaling is not adapted for treatment by means of this drug. If haemorrhage has occurred, or is feared, it is safer to limit the treatment to gargling. If the organism is exhausted and if complications are present, which are not within reach of the drug, no benefit will be obtained. With correct treatment, the result is as follows: Fever, when present apart from complications, usually subsides rapidly. The antipyretic action is specially evident if the fever has been unsuccessfully treated for some time previously. Cough and expectoration are diminished, and, in the majority of cases, disappear entirely after a few weeks. The subjective condition of the patients is rapidly improved and the appetite is markedly increased. In many cases an objective improvement in the pulmonary condition is also manifest, the catarrhal symptoms subsiding or disappearing.

### Protargol.

The use of protargol\*) in ocular affections and in the treatment of gonorrhœa is sufficiently well known. But, according to K. Sitzler, the preparation also deserves consideration in surgery for the treatment of wounds, as is evident from the communications of Floret, Neisser and Strauss. Sitzler describes his clinical experience in this direction. For a number of years he has, with satisfactory results, prescribed protargol in the form of powder to be sprinkled on to sloughing suppurating wounds, especially in pyocyanous infection. According to his instructions, the wounds are first cleansed with an inert substance, such as weak solutions of hydrogen

Jarosch, Deutsche medizinische Wochenschrift 1912, No. 42, p. 1979.

\*) Compare Merck's Reports 1897—1911.

Sitzler, Berliner klinische Wochenschrift 1912, No. 40.

peroxide or aluminium acetate, the surrounding area is freed from dirt by means of benzine or ether and pure protargol powder is then sprinkled on. For reasons of economy, an insufflator is used for this purpose. Then a dressing is applied and is renewed when it is soiled. In a short time, sometimes after the first application, the dressing is no longer stained blue and the offensive pyocyaneus odour has disappeared. The secretion soon ceases, the wound becomes clean and shows satisfactory granulation formation. According to Sitzler, the method of treatment described is superior to the use of moist corrosive sublimate dressings, in that the dressing requires to be changed less often, healing takes place more rapidly and there is less liability to irritation of the wound and of the surrounding area. Protargol is without exception well tolerated, but in sensitive persons its application is followed by a transient burning sensation.

### Prothaemin.

Prothaemin is a preparation made from blood according to E. Salkowski's directions ; it contains the albuminous substances, the iron and the organically combined phosphorus of the blood. It contains about 0·2 p. c. of iron. It is put on the market in the form of a chocolate coloured, fine powder, which is said to be devoid of taste and smell. As indicated by its composition, it is used as a nutrient and strengthening drug, and as a mild iron tonic. P. Korb administered it in pulmonary tuberculosis, anaemia and chlorosis, and in all his cases observed an increase in weight and an improvement in the composition of the blood. The author recommends giving the drug dissolved in milk or cocoa, in amounts of 1 to 2 teaspoonfuls 3 times a day.

Camphausen and Jüngerich obtained equally good results by the employment of prothaemin as those reported by the above named author.

### Pyoktanin.

Further communications on the treatment of foot and mouth disease by pyoktanin have been made by Stilling,

Korb, Deutsche medizinische Wochenschrift 1912, No. 11, p. 513.  
Camphausen, Zeitschrift für Tuberkulose, Vol. 18, No. 5.  
Jüngerich, Fortschritte der Medizin 1912, No. 47, p. 1478.  
Stilling, Landwirtschaftliche Zeitschrift für Elsass-Lothringen 1912,  
No. 23.

Dehne, Kronacher, Oyen and Stietenroth. Stilling again draws attention to the prophylactic employment of the drug\*), by means of which the epidemic can be kept within bounds and the loss which it occasions diminished. The feet and mouths of healthy animals should therefore be treated daily with a pyoktanin solution. Even though it does not give rise to immunity in a strictly scientific sense, still the germs which adhere externally are killed or hindered in their development.

Oyen recommends the following procedure. The feet of the diseased and healthy cattle are bathed in creolin solution, prepared by mixing 1 tablespoonful of creolin with 1 litre of water, and the feet are thoroughly scrubbed with it. When dry, pyoktanin ointment of the following composition is painted on, reaching well above the hind claws: "Pyoktanin 5 parts are mixed with 100 parts of boric acid powder in a mortar and sufficient dilute alcohol is added to produce a thick tough mass on mixing. Then 400 parts of lard are added and finally 500 parts of yellow vaseline. The vaseline must never be added first, for it will then be found impossible to rub up the fat to form a homogeneous ointment." The treatment described is repeated daily for a week.

As the germ of foot and mouth disease enters the animal organism by way of the feet and mouth, Stietenroth advises that these parts be treated with pyoktanin and salt, as common salt augments the action of pyoktanin. Dehne pays special attention to the adequate treatment of the feet, besides irrigation of the mouth and the application of an ointment to the udders. He finds a 1 p. c. pyoktanin solution to be most efficacious; under its influence the ulcers rapidly heal and the wound surface becomes clean and dry. The intense blue coloration makes it possible to tell whether the treatment is being correctly carried out.

Kronacher, as a rule, limits his measures to the thorough cleansing and disinfection of the stable, soft food, dry cleaning of the feet and painting of the clefts of the hoof, the crown

Dehne, Bericht über das Veterinärwesen im Königreich Sachsen für das Jahr 1911, p. 36.

Kronacher, Zeitschrift für Tiermedizin 1912, Vol. 16, No. 3.

Oyen, Berliner tierärztliche Wochenschrift 1912, No. 32.

Stietenroth, Deutsche tierärztliche Wochenschrift 1912, No. 13.

\*) Compare Merck's Report 1911, p. 367.

and the ball with a thick solution of pyoktanin. For the treatment of grave defects of the buccal cavity, it is best to cleanse them with benzine and to treat them with a 10 p. c. pyoktanin solution.

For the treatment of infectious diseases of the feet and tongues of bears, 10 p. c. pyoktanin solution in equal parts of water and alcohol has proved beneficial. According to E. Seifert, the drug soon brings about scab formation and healing, if the animals desist from licking, which is harmful.

Pyoktanin may also be recommended, according to H. Kratzer and Oyen, for the treatment of infectious vaginal catarrh of cows. Kratzer rubs the vaginal mucous membrane, which is studded with nodules, with a rough piece of linen and then paints the raw area once a day with a 10 p. c. alcoholic pyoktanin solution until healing ensues; this usually requires 8 to 20 days. At the same time he has the floor of the cowshed thoroughly disinfected. Oyen prescribed the following ointment:

Rp. Pyoktanin. coeruleum.	5·0 grammes (75 grains)
Acid. boric. pulv.	
Bacillol.	aa 100·0 „ (3½ oz)
Adep. et Vaselin. flav.	aa 400·0 „ (13½ oz)

The vagina was first rinsed with creolin solution; then the above ointment was introduced into the vagina by means of a spatula and cotton wool, and was distributed there. This treatment is to be carried out 3 times on 3 consecutive days, with an interval of one day between each course of treatment.

### Pyramidon.

According to M. John, pyramidon is at least as useful as hydrotherapy in the treatment of typhoid fever. The author tried the drug in 38 severe cases. He brings forward one case which speaks for pyramidon treatment; the administration of several baths a day for a week had failed to remove either the great numbness or the serious circulatory weakness. After the patient had taken 0·15 gramme (2½ grains) of pyramidon every 3 hours for 2 consecutive days, the sensorium became clear and definite improvement was manifest. The author

Seifert, Deutsche tierärztliche Wochenschrift 1912, No. 15.

Kratzer, Münchener tierärztliche Wochenschrift 1912, No. 42.

John, Münchener medizinische Wochenschrift 1912, No. 18, p. 987.

obtained the same effect in 9 other delirious and totally unconscious patients, usually after 2 to 3 days of treatment. The drug only failed in one case, in which there were present large, exceedingly numerous ulcers throughout the ileum and cæcum. Besides this the author lost 3 patients, one from cardiac failure, one from perforative peritonitis and one from intestinal haemorrhage.

As regards the dosage, the author usually prescribed small doses of 0.1 gramm (1½ grains) every 2 hours, or 0.15 gramm (2⅓ grains) every 3 hours, until the temperature and general condition were not markedly altered on tentatively discontinuing the medication for 1 or 2 days. By means of this treatment the majority of cases ran a favourable course, the temperature was as a rule moderately raised up to 37° or 38.5° C. and only in isolated cases was a fall of 2.5—4° C. observed. In consequence of the mild course of the disease, decubitus never ensued.

Hirtz met with sudden falls of temperature in several typhoid patients after doses of 0.15 to 0.2 gramm (2⅓ or 3 grains) of pyramidon in combination with caffeine, and one patient suffered from severe vomiting, so that intestinal perforation might have been suspected. Therefore, during the febrile period, he is in favour of doses not exceeding 0.05 gramm (¾ grain) of pyramidon in combination with caffeine.

### Pyrogallol.

As very good results have been obtained by the application of pyrogallol ointment in lupus, Klara Kennerknecht tried pyrogallol treatment for spina ventosa, with the result that the tuberculous ostitis of the tibiæ was completely healed. The cases dealt with were not only early ones, such as are frequently cured by tonic and climatic influences, but the majority were chronic cases, in which suppuration and fistula formation had occurred. The authoress' method of treatment consists in bathing the diseased limbs for half an hour daily in soap and water and then applying a dressing of pyrogallol ointment. At first a 10 p. c. ointment is used, and if the

Hirtz, Presse médicale 1912, No. 54, p. 573.

Kennerknecht, Münchener medizinische Wochenschrift 1912, No. 10, p. 533.

skin is slightly irritated, a 5 or 2 p. c. ointment. Healing always takes a long time by means of this treatment, about 3 to 4 months when the case is not too advanced, one year or more when fistulas are present. The cosmetic results are said to be highly satisfactory, the fingers returning to their normal size and being once more capable of performing all movements, so that the conservative treatment, requiring so much patience, in spite of its long duration is preferable to operative treatment.

An ointment which is especially useful in chronic infiltrated eczema is, according to Dreuw, prepared as follows:

Rp. Pyrogallol.	20.0	grammes	( $\frac{2}{3}$ oz)
Acid. salicyl.	10.0	"	( $\frac{1}{3}$ "
Liquor. carbon. deterg.	20.0	"	( $\frac{2}{3}$ "
Zinc. oxid.	20.0	"	( $\frac{2}{3}$ "
Sap. moll.	25.0	"	( $\frac{5}{6}$ "
Lanolin. anhydr.	25.0	"	( $\frac{5}{6}$ "

M. Ft. ung. Sig.: Ung. adhesiv.

The greyish-white ointment turns black on exposure to the air, especially on the surface. It is sticky, unlike any other ointment, according to Dreuw, and adheres very firmly to the skin. The ointment is spread on linen or gauze, which is then applied to the affected cutaneous areas. The part of the skin which is stained black by the oxidised ointment is cleaned with benzine. The author never met with irritation of the skin, but under the influence of the ointment he observed the disappearance within 4 to 5 days of localised chronic eczema which had defied all treatment for more than a year.

### Pyrogallol Oxide (Pyraloxin, Oxidised Pyrogallic Acid.)

Pyrogallol oxide is, as its name implies, an oxidation product of pyrogallol (pyrogallic acid), which is prepared by the action of the oxygen in the air on pyrogallol in the presence of ammonia. By the exact regulation of the process of manufacture a uniform preparation is always produced, which is free from unaltered pyrogallol and is insoluble in water. The chemical constitution of the preparation is not known. Pyrogallol oxide dissolves with comparative readiness in alkalies.

Pyrogallol oxide or pyraloxin, as I have mentioned in my previous Reports\*), was suggested by Unna as a substitute for pyrogallol in dermatology. A new, comprehensive paper on this preparation has been compiled by St. von Stein, who used for his experiments both Pyrogallol Oxide Merck and Pyraloxin.

In the first place v. Stein established the fact that pyrogallol oxide is non-toxic. He prescribed it both externally and internally in a large number of different diseases. For application to the eye and to the mucous membranes of the nose and throat, he used a solution of 0.02 grammes ( $\frac{1}{3}$  grain) of pyraloxin in 20 grammes ( $\frac{2}{3}$  oz) of fennel water and 20 grammes ( $\frac{2}{3}$  oz) of a 2 p. c. aqueous solution of borax. The author himself used this solution with good results in conjunctivitis and coryza. Applied in the nose, it brings about anaemia and removes for a brief space the obstruction to nasal breathing. The author has employed the solution with a certain amount of success for instillations and painting in acute and chronic catarrhal rhinitis, atrophic rhinitis, ozæna, dry pharyngitis, chronic catarrhal tonsillitis, catarrhal laryngitis, empyema of the nasal antrum and tuberculous ulcers of the larynx and pharynx. In otology it would, in his experience, come into consideration in chronic purulent otitis media, perforation of the tympanic membrane with buzzing in the ears, affections of the labyrinth, and to promote epithelium formation after complete mastoid operations; but in acute otitis media less is to be expected from it.

The ammonium salt of pyrogallol oxide is of the greatest interest in the treatment of carcinoma; by the internal administration of the drug v. Stein observed a direct influence on the cancerous growth, involving its destruction, checking the development of metastases and acting as a prophylactic on the latter. Externally he prescribed a 5 p. c. ointment made with lanoline, or compresses soaked in a solution of pyraloxin 1:2000; internally he prescribed a 2 p. c. solution of sodium carbonate. Of this, single doses of 1 to 10 grammes (17–170 min.), and daily doses up to 30 grammes (1 oz) were given. Caution is required in tuberculous subjects for

\*) Merck's Reports 1896, p. 132, 1897, p. 125 and 1907, p. 19.

Stein, Praktisches Vratch 1912, No. 5–10. — Zeitschrift für Laryngologie, Rhinologie und ihre Grenzgebiete 1912, p. 879.  
— Münchener medizinische Wochenschrift 1912, No. 46, p. 2529.

whom the author prescribes a far weaker solution (0·1:100 sodium carbonate solution), of which 1 to 10 c. c. (17—170 min.) are administered 3 times a day. On account of the harmlessness of the drug its prophylactic properties may be utilised in suitable cases, in which the development of carcinoma is apprehended, as for example in multiparous women, as they are specially liable to be attacked by uterine carcinoma.

### Quinine.

Th. Müller considers it desirable that careful clinical and pharmacological tests should be carried out on the use of quinine in midwifery as a stimulant of labour pains; for in two cases, which he has described in detail, he obtained remarkably good results. In one case, a woman who had experienced a delay in the commencement of labour during former confinements, on her own initiative took 1 grammie (15 grains) of quinine hydrochloride at 7 o'clock in the morning; at 9 o'clock strong labour pains came on and normal delivery resulted. In another case, two doses of 1 grammie (15 grains) of quinine hydrochloride each, given on one day, sufficed to bring on the delayed labour. H. Rotter, more than a year ago, drew attention to the action of quinine in promoting labour pains. In his experience, quinine acts in three ways, which may be made use of by the obstetrician, viz., as an antipyretic, as an antimycotic, and by stimulating labour pains. The antipyretic action is of use in febrile abortions, in which 0·3 grammie (5 grains) of quinine are given 3 times a day. The antipyretic and antimycotic effects of quinine are seen in puerperal fever. In these cases 0·3 grammie (5 grains) are given 3 times a day for 3 days, in order to assist the organism in its fight against the infective substances. For weak pains 3 doses of 0·3 grammie (5 grains) of quinine are given at intervals of an hour; they may be combined with 0·005 grammie ( $1/12$  grain) of morphine.

Quinine is also of service in obstinate urticaria. In a girl aged 6, who was suffering from urticaria accompanied by severe itching of the skin lesions, which were in part vesicular in character, the usual treatment had proved un-

successful. W. Wolff therefore administered 0.1 grammie ( $1\frac{1}{2}$  grains) of quinine 3 times a day, with the result that the itching disappeared, the vesicles dried up and no new lesions occurred. In 5 other cases of urticaria, quinine, according to the author, proved beneficial.

Sermensan sees promise of good results from quinine therapy in Graves's disease. But the treatment must be continued for a long time, if necessary for years. If small doses do not lead to a cure, larger doses must gradually be given.

For the treatment of pertussis, Heidenhain recommends quinine enemata, together with change of air. An acid-free solution of quinine 2:200 is used, of which 1 to 2 tablespoonfuls, according to the age of the child, are administered rectally 3 times a day.

A. Guillaumin has found that tannate of quinine is excreted far more slowly than the other readily soluble quinine salts. He thinks this fact may prove of use in the indications of quinine. Quinine tannate, among other uses, is said to be of service as a prophylactic in febrile attacks. But it may also be used with advantage in pernicious fever accompanied by sweating, in diarrhoea, night-sweats of phthisis, influenza, pertussis, to reduce arterial blood-pressure, and as a digestive stimulant.

The prophylactic and curative employment of quinine in malaria is discussed by Treutlein, Külz, Faichnie, Hoffmann, Ruge. Külz, in contradistinction to Treutlein, is decidedly in favour of quinine prophylaxis for malaria, as it not possible to set up a mechanical protection against in-

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Wolff, Klinisch-therapeutische Wochenschrift 1912, No. 7, p. 228.  
Sermensan, Klinisch - therapeutische Wochenschrift 1912, No. 38, p. 1124.

Heidenhain, Münchener medizinische Wochenschrift 1912, No. 33, p. 1838.

Guillaumin, Münchener medizinische Wochenschrift 1912, No. 14, p. 790.

Treutlein, Deutsche Medizinal-Zeitung 1912, No. 21, p. 370.

Külz, Archiv für Schiffs- und Tropenhygiene 1912, Vol. 16, p. 475.  
Faichnie, Journal of the Royal Army Medical Corps 1912, Vol. 16, p. 438.

Hoffmann, Berliner klinische Wochenschrift 1912, No. 34, p. 1616.

Ruge, Beiheft zum Archiv für Schiffs- und Tropenhygiene 1912, No. 4.

fection. One gramme (15 grains) of quinine should be prescribed every 8<sup>th</sup> and 9<sup>th</sup> day, or 0·5 grammes ( $7\frac{1}{2}$  grains) every 5<sup>th</sup> and 6<sup>th</sup> day. This medication is, in the author's experience, innocuous, even though transient disturbances may occur. He himself, during several years' residence in the tropics, took altogether 600 grammes (30 oz) of quinine without ill effect and without contracting malaria. According to Hoffmann, on the other hand, fever may supervene even with the most careful prophylaxis, and this measure may cause unpleasant secondary effects. For this reason Ruge is in favour of fractional administration of the requisite doses. He recommends the administration of 1 gramme (15 grains) of quinine every fourth day, taken in separate doses of 0·2 gramme (3 grains), or 0·5 gramme ( $7\frac{1}{2}$  grains) every fourth and fifth day. Hoffmann, based on recent reports, recommends daily doses of 0·25 to 0·3 gramme (4—5 grains) of quinine for prophylactic use; this method is easily carried out and gives rise to no secondary symptoms. Even though it does not offer absolute protection, as was found by Faichnie, yet experience has shown it to be of such benefit that no doubt can be entertained of its value.

Solis-Cohen used quinine dihydrochloro-carbamide with good results in acute lobar and lobular pneumonia. In the form of intramuscular injections, it has a good influence on respiration, improves the general health, alleviates the cough, lowers the temperature and the pulse rate and maintains the strength of the heart and the normal blood pressure. For vigorous persons he recommends initial doses of 1 to 1·6 grammes (15—26 grains) according to the height of the temperature. After an interval of 3 to 4 hours the second injection is given, and if necessary one or two further injections may be given within the first 24 hours. This treatment is continued on the second and third day, so that the patient receives altogether 6 to 10 grammes (90—150 grains) of urea-quinine chloride in 2 to 3 days. From this point on, smaller doses of 0·3 to 0·6 gramme (5—9 grains) a day are administered internally\*). For the injections Cohen uses a 50 p. c. solution of quinine dihydrochloro-carbamide in sterile

Cohen, Medical Times 1912, March. — International Clinics 1912,  
Vol. 3, p. 56. — Semaine médicale 1912, No. 7, p. 78.

\*) Compare Galbraith, Merck's Report 1904, p. 42.

water. The site of injection should be carefully disinfected, in order that no local symptoms of irritation may occur. The same method is, according to Castaigne, of some use in cancer, in which it brings about improvement of the general health and alleviates the pain. For its use in this indication the author prefers the more soluble quinine salts, such as quinine dihydrochloride, hydrochloride and formate in 10 p. c. solution, 2 to 3 c. c. of which are injected on alternate days. At the same time 0·5 gramm (7½ grains) of quinine is given by mouth twice a day. Of course, no lasting effect nor cure is to be expected from this treatment, but it aids in alleviating the great distress experienced by the patient and enables him to follow his occupation for a little while longer.

In my last year's Report, I mentioned the value of quinine as a local anaesthetic. Schepelmann has made further studies of this method of anaesthesia, and has had his quinine-antipyrine-adrenalin solution put on the market in ampoules under the name of "sinecain". This preparation is intended for subcutaneous injection; it is not at present suited, according to the author's experience, for lumbar use. Sinecain is said to be of special service in prolonging the period of local anaesthesia by cocaine, without exceeding the maximum dose of cocaine. It is contra-indicated in ill-nourished, tense tissues, in which there is the possibility of injuring the cellular tissue and retarding the healing of the wound.

With regard to the anaesthetising action of quinine salts, reference may be made to the investigations of J. Morgenroth and S. Ginsberg. The authors applied a 3 p. c. aqueous solution of quinine hydrochloride to rabbits' eyes, and found that at the end of 1½ minutes it produced complete anaesthesia lasting for about an hour. More dilute solutions were less efficacious.

J. Davidson reports upon several cases of uterine prolapse, in which he adopted Parson's method of injecting quinine sulphate solution into the broad ligaments. The results

Castaigne, *La clinique* 1912, No. 25.

Schepelmann, *Medizinische Klinik* 1912, No. 43, p. 1743.

Morgenroth-Ginsberg, *Berliner klinische Wochenschrift* 1912, No. 46, p. 2184.

Davidsohn, *British Medical Journal* 1912, II. p. 233.

were good, for out of 6 cases which were seen after months and years, only one showed a relapse.

### Sabromin.

According to S. Szabo, sabromin\*) possesses the satisfactory property of not upsetting the stomach, and it can in consequence be used for months without apprehension. The author also considers its tastelessness to be a great advantage. Secondary effects, such as bromism, rarely occur after its employment, and the author never met with bromine acne, even after the administration of large doses.

Szabo prescribed 3 tablets a day for 6 months for a 10-year-old boy suffering from epilepsy, and he showed no antipathy to the drug. During this period no attacks occurred and the child's physical development was satisfactory. On continuing the medication, an attack only occurred every 3 to 4 months. This case shows that sabromin is well tolerated and is efficacious, which is probably due to the slow excretion of the drug.

### Safranine.

L. Brieger and M. Krause have continued the experiments of Weber and Krause. The last named authors had found that fuchsine I a DT, given to animals infected by trypanosomes prolongs life and effects the disappearance of trypanosomes from the peripheral circulation. As the subcutaneous injection of dyes is usually very painful to human beings, Brieger and Krause sought a nitrogenous dye, which on internal administration destroys trypanosomes. They believe that they have now found substances of this nature in the safranine group. They succeeded in demonstrating that rats, which had been infected with a strain causing death within 48 to 72 hours, were kept free from trypanosomes for about 3 months by the internal administration of safranine. The safranines possess a bitter taste, but are non-toxic for man and animals. The medication did not give rise to albuminuria or other ill-effects, nor was the appetite disturbed. Even

Szabo, Pester medizinisch-chirurgische Presse 1912, No. 12.

\*) Compare Merck's Reports 1903, 1904 and 1910.

Brieger-Krause, Berliner klinische Wochenschrift 1912, No. 2, p. 60.

Weber-Krause, Merck's Report 1907, p. 111.

when daily doses of 1 gramme were given to man, they produced no disturbance of the general health. The authors state that experiments are now being carried out on people living in the parts of Africa in which sleeping sickness prevails.

### Salen.

Salen is a mixture of ethyl and methyl glycolic acid esters of salicylic acid; it is an odourless liquid, which dissolves readily in alcohol, ether, benzine and castor oil, and only slightly in olive oil. A. Eibig has prescribed the preparation with satisfactory results in acute and chronic rheumatism. According to his instructions, it is painted or rubbed on either pure or mixed with alcohol ( $1+1$ ) or chloroform oil. It is applied 3 times a day, and, after being rubbed, the affected parts are covered with cotton wool or flannel. At the same time 4 doses of 1 gramme (15 grains) of salipyrin a day are given internally. By this means the author effected a cure in acute rheumatism and alleviation of the pain with marked improvement in chronic rheumatism. Salen is also beneficial in sprains, in which its application is supplemented by massage and warmth.

### Salvarsan.

The fact is being ever more recognised that a really new and efficacious method of treatment demands sacrifices during the period of its introduction, as is shown by many examples in the history of medicine. Even though salvarsan has not been accepted with enthusiasm by all, because at first too much was expected and perhaps also promised with regard to it, yet every impartial student of salvarsan therapy must admit that the greatness of Ehrlich's discovery is indisputable. The greatest interest connected with salvarsan therapy lies in the treatment of syphilis, though better results have undoubtedly been obtained by its employment in other diseases. This is natural, considering the wide distribution and the great dangers of syphilis as a scourge of the human race, whereas diseases like framboesia, relapsing fever, chorea, pellagra, etc., are of but secondary importance.

The fact that salvarsan is an efficacious remedy in syphilis requires no further discussion; it is also clearly manifest from

a large number of publications during the past year. Further investigations will, therefore, have to deal only with the technical side of its employment, with which is connected the avoidance of dangers and of by-effects; for the value of salvarsan as a remedy with a permanent effect can only be definitely settled in the course of decades. The importance of technique in the employment of salvarsan is shown, among other matters, in the communications by Ehrlich and Wechselmann. Wechselmann reports that he administers about 1000 injections a month to in-patients and out-patients and does not hesitate to repeat the injections in suitable cases. He prescribes doses of 0·5 and 0·6 grammes without ill-effect, which he ascribes to his faultless technique. In opposition to the view of other observers, he insists upon the employment of distilled water free from bacteria for the solution of salvarsan. Like Ehrlich, he attaches great importance to the avoidance of the so-called water error. But with regard to other technical points of intravenous salvarsan injection also, practice will lead to the desired end. Preliminary examination and exact observation of the patients will add much to the elimination of by-effects. It is, according to Wechselmann, becoming ever more evident that when the correct employment of salvarsan gives rise to a reaction, the cause lies in some pathological condition of the individual under treatment. The author has scarcely met with nervous relapses during the last eighteen months. His statement with regard to the action of salvarsan on the optic apparatus is of special significance: "I should like to emphasise the fact that out of about 25,000 injections, not a single injury to the optic apparatus occurred, whether this were healthy or diseased." With regard to fatal cases following salvarsan injections, Wechselmann may be considered to have proved that such are due to individual characteristics. In the only case of death from salvarsan which has occurred in the author's practice, he attributes the cause of death to the combined treatment with salvarsan and mercury, and this might also be proved in almost all other fatal cases described. This probably shows that in the combined treatment, which has recently been recommended by many investigators and doctors, special attention should be directed to the organs which excrete the urine.

Besides the secondary effects due to the water error, thromboses have been observed. Local thromboses are oc-

casioned, according to Ehrlich, by too great alkalinity of the injection fluid; the "distant thrombi" are presumably due to preceding mercury injections; they may therefore be avoided. The author further points out that if there is a suspicion of syphilitic processes of the nervous system, only small doses of salvarsan (0·1 to 0·3 grammes) should be injected. Ehrlich is in favour of combined treatment by salvarsan and mercury and of the repeated injection of salvarsan.

With regard to the method of administration of salvarsan, intravenous injection has generally been employed. For intramuscular injection Schindler's preparation "Joha" has proved of some value. It is reported upon by Schmitt, Stroscher, Schindler, Steiger and Lindenheim. According to these communications, Joha (an emulsion of salvarsan and iodipin), on the whole, offers similar advantages to salvarsan. It exercises a favourable influence in a short time on syphilis of the skin and mucous membranes, and on malignant syphilis, and if properly employed, it is non-injurious. As it is put on the market ready for use, it is perhaps of greatest interest for ambulant treatment. Like salvarsan, it is contra-indicated in cardiac disease, or should at least be used with caution.

As to the dosage of salvarsan, there is nothing special to be added to my former reports. Reference, however, may be made to a communication by Engelmann on its dosage for children. Here, also, the author is in favour of its intravenous employment (into the cubital vein). He considers that in severe infections not less than 0·04 grammes should be given to sucklings, and even 0·1 gramme is well tolerated by young babies. The injection may be repeated or may be supplemented by other suitable drugs.

The indications for salvarsan (old and new) may be noted from the appended bibliography. The space allotted to my Reports forbids a more detailed description. It may be noted that salvarsan has also proved very valuable in veterinary

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Schmitt, Münchener medizinische Wochenschrift 1912, No. 13, p. 694.  
Stroscher, Münchener medizinische Wochenschrift 1912, No. 18,  
p. 986.

Schindler, Deutsche medizinische Wochenschrift 1912, No. 20, p. 948.  
Steiger, Münchener medizinische Wochenschrift 1912, No. 37, p. 2000.  
Lindenheim, Berliner klinische Wochenschrift 1912, No. 46, p. 2178.

— Münchener medizinische Wochenschrift 1912, No. 41, p. 2233.  
Engelmann, Zentralblatt für Gynäkologie 1912, No. 3, p. 65.

medicine in the treatment of contagious pneumonia of horses, as has been reported by Rips, Nevermann, Gordsjalkowsky, Osebe, Jacob and Kettner. The importance of salvarsan in this disease lies in the fact that every case can be cut short by a single infusion of 0·01 grammes for each kilogramme of body-weight, administered before the disease reaches its height. The dreaded complications of the disease are also avoided by this treatment. For the infusion a solution of 1:30 to 100 of distilled water or normal saline solution is used. Favero used salvarsan for covering disease of dogs; at the height of infection he injected a dose of 0·12 grammes intravenously for each kilogramme of body-weight. The parasites are rapidly destroyed and the disease can be checked during the incubation period by the simultaneous intraperitoneal application of virus and salvarsan. Salvarsan is also used in foot and mouth disease. According to Miessner, although it is unable to prevent the spread of the disease, it apparently mitigates the character of the epidemic. In chicken cholera Schaburow undertook experiments which showed that a single injection of 0·0035 grammes for every kilogramme of body-weight effects the cure of fowls and geese. The value of the drug as a prophylactic is insignificant, as its action only lasts for 3 days. In glanders of horses, salvarsan is apparently of no use. Blagodetelew's investigations have at least shown that the favourable influence exercised on the disease by the drug is delusive.

Like last year, I append a list of references to salvarsan literature; it contains the more important communications concerning this preparation, without claiming to be absolutely complete.

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Rips, Berliner tierärztliche Wochenschrift 1911, No. 7, p. 113.  
Nevermann, Berliner tierärztliche Wochenschrift 1912, No. 7, p. 119  
and No. 14, p. 241.  
Gordsjalkowsky, Veterinarny Wratsch 1912, No. 18.  
Osebe, Allatorvosi lapok 1912, No. 21.  
Jacob, Zeitschrift für Veterinärkunde 1912, Vol. 23, p. 406.  
Kettner, Berliner tierärztliche Wochenschrift 1912, No. 46.  
Favero, Clinica veterinaria 1912, No. 4.  
Miessner, Archiv für Tierheilkunde, Vol. 37, No. 6. — Berliner  
tierärztliche Wochenschrift 1912, No. 27.  
Schaburow, Berliner tierärztliche Wochenschrift 1912, No. 43.  
Blagodetelew, Berliner tierärztliche Wochenschrift 1912, No. 35.

**Acanthosis nigricans:**

Bonnet, Lyon médical, Vol. 118, No. 13.

**Anæmia (pernicious) and Pseudoleukæmia:**

Friedländer, Journ. Americ. Med. Assoc. 1912, No. 6. — Curschmann, Münchener med. Woch. 1912, No. 29, p. 1613. — Perussia, ibid. 1912, No. 27, p. 1482. — Valladi, ibid. 1912, No. 27, p. 1483. — Hobhouse, Brit. Med. Journ. 1912, 14<sup>th</sup> Dec.

**Angina Vincenti:**

Sourdel, Münchener med. Wochenschrift 1912, No. 7, p. 394.

**Anthrax:**

Becker, Med. Klinik 1912, No. 44, p. 1790. Deutsche med. Woch. 1912, No. 12, p. 545. — Bettmann-Laubenheimer, Deutsche med. Woch. 1912, No. 8, p. 349. — Schuster, Münchener med. Woch. 1912, No. 7, p. 349.

**Bacterial Infections:**

Bierbaum, Deutsche med. Woch. 1912, No. 43, p. 2012. — Ruhe-mann, Med. Klinik 1912, No. 12, p. 486.

**Banti's Disease:**

Perussia, Münchener med. Woch. 1912, No. 27 and 29.

**Bilharzia:**

Day-Richards, Lancet 1912, April, No. 4626. — Fülleborn, Werner, Deutsche med. Woch. 1912, No. 8, p. 351. — Loos, ibid. 1912, No. 2, p. 70.

**Bubonic Plague:**

Amann, Deutsche med. Woch. 1912, No. 46, p. 2166.

**Chorea:**

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#### Sandal Wood Oil.

This well known antigenorrhœic forms the chief constituent of two recently introduced preparations, gonaromat and blenotin.

Gonaromat is Sandal wood oil with the addition of mace oil, oil of chamomile, cinnamon oil, oil of peppermint and oil of cloves, which increase the tolerance towards the remedy. Witte states that not one of his patients was troubled by oily tasting eructations, while the preparation had a beneficial influence on the appetite. But this favourable characteristic, which is confirmed by R. Polland, is probably largely dependent upon the nature of the capsules in which gonaromat is put on the market, for these do not dissolve until they reach the intestine. Nor did the authors observe other undesirable secondary symptoms, such as renal irritation. On the other hand, the drug possessed the well known property of sandal wood oil of rendering the urine clear, which made it possible after a brief medication to pass to the local treatment of gonorrhœa. Nocturnal erections and painful scalding in the bladder also disappeared. 6 to 9 capsules are administered as a daily dose.

Blenotin contains other active substances besides sandal wood oil and these may be of use in inflammation of the urinary passages. According to F. Berger, one capsule contains 0.16 grammes of sandal wood oil, 0.02 grammes of myrrh,

Witte, Allgemeine medizinische Zentralzeitung 1912, No. 37.

Polland, Österreichische Ärzte-Zeitung 1912, No. 11.

Berger, Medizinische Klinik 1912, No. 17.

0·02 grammie of camphor, 0·12 grammie of hexamethylenetetramine, 0·11 grammie of boric acid and 0·02 grammie of mushroom extract. The author prescribed the preparation with good results in acute gonorrhœa of the urethra, in gonorrhœal cystitis and in infantile gonorrhœa. No case showed undesirable secondary effects on the part of the gastro-intestinal tract, or albuminuria. The secretion was diminished on the second or third day in some cases, but usually at the end of a week and disappeared in the course of 10 to 14 days. At the same time the urine became clear and the gonococci and the subjective symptoms disappeared. The author administered 2 capsules 4 times a day.

### Santonin.

D. J. Drake having pointed out that chromosantonin, the yellow product obtained by the action of sunlight on santonin, and which is no doubt isomeric with santonin, is of special efficacy in tropical dysentery, Begg and Maxwell attribute the entire action in dysentery to chromosantonin. Like Drake, they consider that the preparation should be administered in oily solution, as it is most efficacious in this form. Drake usually administered 0·3 grammie (5 grains) of chromosantonin in 8 grammes (150 min.) of olive oil 3 times in the course of 24 hours.

### Santyl.

I have previously pointed out\*) that santyl is a very effective drug for removing the troublesome acute inflammatory symptoms in gonorrhœal affections of the urethra, thus acting as a preliminary to local treatment. This experience is confirmed by the communications of O. Nitze, who has employed the drug with complete success in a number of cases of acute and chronic gonorrhœa. The author attaches the greatest importance in the treatment of gonorrhœa to the local application of silver; but santyl medication, if employed sufficiently early, soon removes the burning sensation in the urethra and the pricking pain and thus gives the patients

Drake, Merck's Report 1907, p. 203.

Begg-Maxwell, Pharmaceutical Journal 1912, Vol. 88, p. 808.

\*) Compare Merck's Reports 1905—1911.

Nitze, Therapie der Gegenwart 1912, No. 8, p. 381.

confidence in the treatment. In one case of long standing chronic gonorrhœa, besides local treatment by protargol, Nitze administered to the patient over 200 santyl capsules without any complaint being uttered. The patient's condition was permanently improved, the discharge ceased, the stricture disappeared, the urine became clear and was passed without pain. Special interest attaches to the author's observation that santyl is also beneficial in non-gonorrhœal affections of the bladder. He prescribed santyl for a woman who had for very many years suffered from leucorrhœa and menstrual disturbances as well as from vesical trouble; as a result, her trouble on passing water disappeared. In a case of chronic catarrh of the vagina and of the uterus, accompanied by severe cystitis and purulent urine, in which irrigation of the bladder with potassium permanganate solution had proved ineffectual, he administered santyl for a prolonged period (about 100 capsules), with the result that the violent vesical symptoms subsided in a comparatively short time and the urine became clear.

According to A. Piersig, santyl is deserving of special mention among the modern balsams because, while efficacious, it is free from unpleasant secondary effects. Burning in the urethra, painful erections and scalding in the bladder are very favourably influenced and removed by the preparation.

J. Josephsohn gave only santyl without local applications for 4 or 5 days or longer in gonorrhœa, and obtained very satisfactory results in anterior urethritis by this means. It also proved beneficial in posterior urethritis, in which it reduced the swelling of the inflamed tissue, cleared the urine and improved the subjective symptoms; and it proved beneficial in a neurasthenic patient, who complained of all sorts of abnormal sensations in the urethra after the gonorrhœa had been cured.

### Scarlet Red.

Scarlet red has proved of special value as an epithelium forming remedy, in the form of so-called scarlet red ointment, as I have previously pointed out here\*). O. Retzlaff ob-

Piersig, Reichs-Medizinal-Anzeiger 1912, No. 5.

Josephsohn, Medico 1912, No. 9.

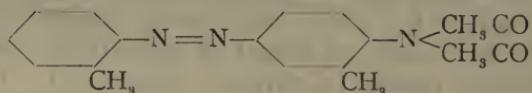
\*) Compare Merck's Reports 1908—1911.

Retzlaff, Deutsche medizinische Wochenschrift 1912, No. 42, p. 1984.

tained very satisfactory results by the use of this ointment in extensive burns and corrosions, in which transplantation could not be carried out. In the author's experience, a great advantage of scarlet red treatment is the formation of normal skin and not of scar tissue. While Schmieden regards as a condition of successful treatment the healthy character of the granulations in conjunction with the absence of inflammation, the ointment can also be applied to discharging wound areas. In large areas, in which copious secretion is still taking place, small islets may frequently be observed in the midst of the wound area, and it is from these centres that the further formation of epithelium takes place. A suitable remedy for loose and glassy granulations, such as may occur under the action of scarlet red, is boric ointment or silver nitrate ointment (1 to 2 p. c.); it is also useful if, towards the end of treatment, small granulating areas are no longer affected, or are only very slowly affected by scarlet red ointment. After the application of silver ointment, the action of the dye is once more plainly manifest.

Retzlaff describes two new substances, chemically related to scarlet red or amido-azotoluol\*), viz., pellidol and azodolen.

Pellidol is diacetyl-amido-azotoluol, having the chemical formula:



It forms bright, brick-red needles, melting at 65° C., or thick, red crystals, similar to potassium bichromate, with a melting point of 75° C. The commercial product is a pale, reddish-yellow powder, without staining capacity. Soiling of the linen or hands caused by its use can be removed with soap and water. The preparation is insoluble in water, but dissolves readily in alcohol, acetone, chloroform, ether, benzol, vaseline and fatty oils. If correctly prepared, therefore, pellidol ointments form solutions of the drug and not suspensions, as is the case with scarlet red ointment. They are consequently more efficacious and may be used in correspondingly lower concentrations.

Schmieden, Zentralblatt für Chirurgie 1908, No. 6.

\*) Compare Merck's Reports 1909—1912.

Azodolen is a mixture of equal parts of pellidol and iodolen (iodol-albumin compound, compare Merck's Reports 1900 and 1901, or Merck's Index 1910, p. 152), a pale yellow powder, which besides promoting the formation of epithelium, also acts as an antiseptic.

Like Schmieden, Retzlaff also considers that in extensive burns and corrosions, transplantation is of primary importance. But if this is refused or if it is not entirely successful, a 2 p. c. pellidol ointment (prepared with vaseline) will furnish a useful remedy in all cases requiring the formation of epithelium over wound areas. A 2 p. c. pellidol-kaolin may also be recommended. This mixture gave an excellent result in a case of varicose ulcer of the leg. In this case a thin epithelial layer had formed over the ulcers in a few days and this soon led to definite skin formation. The author also obtained good results by the use of azodolen, which gave promise of its successful employment for syphilitic ulcers.

C. Decker and Bantlin obtained very satisfactory results in burns, wounds and ulcers of the leg by the use of pellidol and azodolen. Decker extols the cleanliness of its employment as compared with scarlet red.

### Scopolamine Hydrobromide.

As a result of a pharmacological investigation, H. Langer came to the conclusion that the very dilute solutions of scopolamine hydrobromide, which are issued in ampoules, lose their effect to a considerable degree on keeping. He therefore demands that the scopolamine solutions required for subcutaneous administration should always be freshly prepared. This requirement may be complied with without hesitation, because it will render the procedure reliable and free from objection in all cases, whether or not the scopolamine solution deteriorates in value for clinical purposes on keeping. It is evident from the communications of F. Sachs, E. Hug and R. Willstätter that the question as to whether and how scopolamine in aqueous solution undergoes alteration has

Decker, Medizinische Klinik 1912, No. 49, p. 1990.

Bantlin, Münchener medizinische Wochenschrift 1912, No. 39, p. 2107.

Langer, Therapeutische Monatshefte 1912, No. 2, p. 121.

Sachs, Berliner klinische Wochenschrift 1912, No. 30, p. 1415.

Hug, Archiv für experimentelle Pathologie 1912, Vol. 69, p. 45.

Willstätter-Hug, Zentralblatt für Physiologie 1912, Vol. 26, p. 167.

not yet been definitely settled. Hug, in opposition to Langer, found that a scopolamine solution does not alter on keeping and that its efficacy is not diminished; Sachs, however, assumes that the efficacy of a scopolamine solution diminishes in one direction, e. g., as an antagonist to muscarin, and remains unaltered in another direction, e. g., in its central paralysing action. It is therefore conceivable that a scopolamine solution may retain its clinical value even after having been kept for a prolonged period, but suitable experiments are required to establish this assumption.

During the past year a number of authors have reported upon the use of injections of scopolamine and morphine, or of omnopon, to supplement general anaesthesia. F. Brunner admonishes caution, for in one case he met with threatening symptoms after the administration of 0.04 gramme of omnopon and 0.0004 gramme of scopolamine, and he attributes the death of the patient to the scopolamine. As a supplement to ether or chloroform inhalation anaesthesia, he is therefore in favour of small doses of omnopon — 0.02 gramme — and scopolamine (0.00075 to 0.001 gramme for men and 0.00025 to 0.0005 gramme for women). It is noteworthy that the author, in opposition to the view of Helmberger and others, does not consider omnopon superior to morphine. Like Sick, he is of opinion that scopolamine should first be injected and then omnopon or morphine (the scopolamine being repeated if necessary), in order that it may not first take effect during the inhalation anaesthesia and thus act cumulatively and become dangerous. Scopolamine being somewhat widely employed, unfortunate accidents following the use of pure scopolamine hydrobromide and of a freshly prepared solution are probably entirely or for the most part due to the individuality of the patients and not to the scopolamine. This is manifest in a communication by R. Zimmermann; a patient was given 0.007 gramme by mistake, i. e., 14 times the maximum dose and, by means of suitable treatment (subcutaneous injection of 1000 c. c. of 0.85 p. c. saline solution), recovered in a short time without harm. Various observers have pointed out that caution is necessary in the case

Brunner, Münchener medizinische Wochenschrift 1912, No. 3, p. 134.  
Helmberger, Österreichische Ärzte-Zeitung 1912, No. 6, p. 91.  
Zimmermann, Münchener medizinische Wochenschrift 1912, No. 8,  
p. 423.

of elderly people. Brüstlein reports that the latter only require very small doses. Sensitive elderly women are given 0.0003 grammes of scopolamine hydrobromide and 0.03 grammes of omnopon in two portions with an interval of 10 minutes, three quarters to one hour before the operation. In alcoholic subjects caution should be exercised, or it may be best to avoid injection anaesthesia. Pflugk draws attention to the possibility of glaucoma being brought about by the employment of scopolamine for the induction of dawning sleep.

Further communications relating to the employment of scopolamine in combination with morphine or omnopon, or of scopomorphine, for the production of anaesthesia or dawning sleep\*) have been made by Colmers, J. Fleischner, Stenglein, Rousseau, Putyatina, P. Müller, M. Cazin, H. Offergeld, L. A. Diawatin, R. Mühsam, B. Agricola, M. Kähler (for anaesthesia), B. Bosse, Biermer, W. Feodorow, A. Reinhart, O. Jaeger and Zweifel (for dawning sleep or childbirth).

Scopolamine is very efficacious in treatment of the morphine habit. It is of special service towards the end of the

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Brüstlein, Korrespondenzblatt für Schweizer Ärzte 1912, No. 10.  
Pflugk, Klinische Monatsblätter für Augenheilkunde (N. F.) Vol. 12.

— Deutsche medizinische Wochenschrift 1912, p. 677.

\*) Compare Merck's Reports 1902—1911.

Colmers, Zentralblatt für Chirurgie 1912, No. 8, p. 253.

Fleischner, Münchener medizinische Wochenschrift 1912, No. 23, p. 1263.

Stenglein, Deutsche Zeitschrift für Chirurgie 1912, Vol. 114, No. 5/6.

Rousseau, Presse médicale 1912, No. 54, p. 573.

Putyatina, Zentralblatt für Gynäkologie 1912, No. 28, p. 927.

Müller, Beiträge zur klinischen Chirurgie 1912, Vol. 79, No. 1.

Cazin, Therapeutische Monatshefte 1912, No. 8, p. 599.

Offergeld, Deutsche medizinische Wochenschrift 1912, No. 50, p. 2362.

Diawatin, Zentralblatt für Chirurgie 1912, No. 51, p. 1729.

Mühsam, Medizinische Klinik 1912, p. 975.

Agricola, Klinische Monatsblätter für Augenheilkunde 1912, p. 187.

Kähler, Zeitschrift für ärztliche Fortbildung 1912, No. 8, p. 237.

Bosse, Monatsschrift für Geburtshilfe und Gynäkologie Vol. 33, No. 3.

Biermer, Zeitschrift für ärztliche Fortbildung 1912, No. 17.

Feodorow, Praktitscheskij Wratsch 1912, No. 7/8.

Reinhart, Klinisch-therapeutische Wochenschrift 1912, No. 33, p. 959.

Jaeger, Deutsche medizinische Wochenschrift 1912, No. 24, p. 1141.

Zweifel, Münchener medizinische Wochenschrift 1912, No. 15, p. 844.

cure, in passing from small doses of morphine, to which the morphinomaniac has been reduced without difficulty, to total abstinence. A. Fromme employs in these cases a so-called "protracted scopolamine narcosis", which consists in keeping the patient in bed and continuing the administration of subcutaneous injections of scopolamine hydrobromide (Merck) day and night until all symptoms due to discontinuation of morphine have disappeared. The greater the dose of morphine to which the patient has become accustomed, the longer must the narcosis be continued, in slight cases 3 to 4 days, in severe cases 7 to 8 days. According to Fromme, the morphine product present in the organism must be completely neutralised and excreted by means of the scopolamine treatment, after which the patient no longer feels the desire for morphine nor for scopolamine. Morphine must not be administered together with scopolamine. The patient is to be kept in a dark room during treatment, to have milk diet, and the dryness of the throat and the thirst are relieved by means of mineral water. The narcotised patients must be constantly watched and the author furnishes a number of other instructions, for which reference must be made to the original paper. To obtain a good result comparatively large doses of scopolamine are required, and, according to Fromme, a morphinomaniac will tolerate more than a normal individual, even up to 10 times the maximum dose. Injections of 1.5 to 2 milligrammes are usually given, but the author has given as much as 1.5 centigrammes in the course of 24 hours, without meeting with any unwelcome sequelæ in many years of practice. As, according to the author, practice and experience are required in order to carry out the method of protracted scopolamine narcosis described, it is at present only suitable for institutional treatment. Here it should be productive of reliable and permanent results.

### Sedobrol.

In order that the administration of bromine and dechlorination in the treatment of epilepsy may be made as acceptable as possible, R. Ammann recommends a combination of sodium bromide with vegetable extracts, which

is put on the market in the form of tablets. The preparation is intended to be made into soups. As the taste of soup is not pleasant without salt and with the addition of sodium bromide, vegetable extracts were added, as they have an aromatic taste and thus conceal the want of salt. The author states that by pouring hot water over sedobrol, a tasty bromine broth is produced, which is well suited for the treatment of epileptics. Three tablets, corresponding to 3 grammes (45 grains) of sodium bromide, are given for a daily dose. As sedobrol tablets do not give rise to gastric disturbance, they are well adapted for a course of bromine treatment. Should this medication prove insufficient, 0.3 to 1 gramme (5—15 grains) of chloral hydrate is given every evening immediately before retiring to rest (especially for nocturnal attacks). The patients should pay special attention to the care of the mouth, in order to eliminate stomatitis with foul breath to which bromine may give rise. For this purpose a good mouth wash with the addition of a little common salt is used, as for example a solution of 1 gramme (15 grains) of potassium permanganate and 50 grammes ( $1\frac{2}{3}$  oz) of sodium chloride in 1000 grammes ( $3\frac{1}{3}$  oz) of water, 1 teaspoonful of which is added to a glass of water for use. Treatment by sedobrol is suitable for neurasthenics as well as for epileptics, as has been confirmed by H. W. Maier.

### Sennatin.

Sennatin is a fluid extract prepared from senna leaves, which contains the aperient principles of the drug without producing their secondary effects. The preparation has a specific gravity of about 1.045—1.075, it yields about 1 to 2 p. c. of ash and leaves a dry residue of 10 to 12 p. c. It gives the reactions characteristic of the group to which emodin and chrysophanic acid belong. It occurs as a dark, clear, stable and sterile fluid, which is so thin that it can readily be given without apprehension by subcutaneous and intramuscular injection. B. Credé has used this preparation with good results in nearly 300 cases of constipation of all varieties, of intestinal paralysis and of meteorism. According to the author's observations, sennatin

Maier, Münchener medizinische Wochenschrift 1912, No. 36, p. 1950.  
Credé, Münchener medizinische Wochenschrift 1912, No. 52, p. 2868.

is totally non-toxic and in doses of 5 grammes (90 min.), it causes neither general unpleasant effects nor renal irritation. It stimulates intestinal activity so strongly in every case that powerful evacuations of intestinal gases ensue, and that in those cases in which the mechanical obstruction is not too considerable, stimulation of the large intestine effects evacuation of the bowels also.

Injections of sennatin have proved beneficial in intestinal paralysis, in infections, in peritonitis and in intestinal obstruction. After abdominal operations and operations for hernia, if intestinal gases have not been spontaneously evacuated, Credé injects 2 grammes (34 min.) of sennatin on the evening of the operation or on the following morning. No injection of sennatin should, however, be given during or shortly before an injection of scopolamine-morphine, because morphine interferes with the action of sennatin. But the injection shows a good effect 5 to 6 hours after operation. If no evacuation of the bowels ensues, the treatment must be supplemented by glycerin enemata.

A single dose of sennatin consists of 1 to 3 grammes (17—50 min.). Adults are usually given 2 grammes (34 min.), which is sufficient in most cases. For subcutaneous injection a very lax part of the skin must be chosen and the injection must be given slowly to avoid cutaneous irritation. Intramuscular injection, which is preferred by the author, is applied into the most external part of the gluteal muscle.

## Sera and Antigens.

### Antithyroidin Moebius.

Antithyroidin is beneficial even in severe cases of Graves's disease. A further proof of this\*) has been furnished by Blanchod, who obtained a noteworthy result in a case of this kind accompanied by nervous disturbances, by the administration of large doses. Even the first series of doses gave a satisfactory result, but on discontinuing the medication the symptoms recurred at the end of a fortnight. As great lassitude and respiratory troubles were experienced

\*) Compare Merck's Report 1896—1911.  
Blanchod, Province médicale 1911, No. 49.

and treatment by X rays was not possible, the author tried another course of antithyroidin. This time definite improvement was observed after the first week of treatment, for the patient showed increased appetite and a gain in weight and was able to mount steps without much difficulty. On the 10<sup>th</sup> day of the medication the pulse rate had fallen from 150 to 75, and on the 20<sup>th</sup> day the patient was able to resume his occupation. On account of too early discontinuance of the administration of antithyroidin, the patient's condition again grew worse and a prolonged course of antithyroidin treatment was commenced. By this means Blanchod effected a cure. It is clearly manifest from this case that antithyroidin takes effect with comparative rapidity, but that on completion of one course of administration its employment should not be discontinued for too long a period. That the beneficial effect is due to the drug itself and not to any other chance circumstances is shown by the return of the symptoms on the discontinuance of the medication, and the improvement following renewed medication, which occurred concurrently.

Among other cases benefited by antithyroidin, E. Verde reports upon a case of Graves's disease, accompanied by symptoms which gave rise to much anxiety. After a month's administration of antithyroidin these had improved considerably, and after further treatment for 3 months the patient's condition had returned to normal.

H. Schlesinger, as the result of his experience, considers the administration of antithyroidin of very great importance in addition to other therapeutic measures. He usually prescribes 1 tablet, or 15 to 20 drops of the fluid preparation, 3 times a day. At the same time he prescribes a daily intramuscular injection of 0·02 to 0·5 gramme ( $\frac{1}{3}$ — $7\frac{1}{2}$  grains) of sodium cacodylate for 30 days. The drug therapy may with advantage be supplemented by X ray treatment.

A case reported by A. Hougaard of acute Graves's disease in a boy aged 14 is of special interest. The dose was gradually increased from 15 to 30 drops, the general condition was considerably improved, the tachycardia and tremor were much diminished and the exophthalmus disappeared almost completely. The goitre alone remained unchanged.

H. Alamartine, who also considers antithyroidin medication to be a most useful measure, recommends a trial with antithyroidin treatment before operative measures.

### Pneumococcus Serum Merck.

Reference may first be made to some communications on pneumococcus serum which have not previously been discussed.

Gläser reports that by the use of pneumococcus serum Merck he succeeded in protecting guinea-pigs against fatal doses of pneumococci. Details of 11 very severe cases of pneumonia treated by Merck's pneumococcus serum appeared in the *Sanitätsbericht über die königlich preußische Armee* (Mittler 1911). In every case considerable improvement in the general health occurred 6 to 10 hours after the injection of the serum, and in 6 cases there was a pronounced feeling of well-being. The pains ceased, the patients became calm and interested, the temperature fell by lysis 10 to 12 hours after the injection, no crisis was observed and the process made no advance.

Sill's results with pneumococcus serum in children, though not "brilliant", were manifestly favourable in some cases.

Weitz and Géronne obtained good results by the use of Neufeld's serum; very large intravenous doses (up to 100 c. c.) of this serum were required to give a definite result, as manifested by shortening of the febrile period and a beneficial influence on the general health. With regard to Merck's serum the following statement appears in the paper by Géronne: Seeing that the most varied opinions have been held with regard to Römer's pneumococcus serum, some speaking of its extraordinarily favourable, almost definitely specific influence, whilst others (and these form the great majority) have met with no success and do not look upon its employment as harmless, we have not as yet felt justified in employing intravenous injections of Römer's serum. I am, however, obliged to explain that Géronne's statement that the majority of authors have been unsuccessful in their employment of Römer's

Alamartine, *Gazette de hôpitaux* 1911, No. 148, p. 2119.

Gläser, *Deutsche tierärztliche Wochenschrift* 1910, No. 46.

Sill, *Medical Record* 1911, p. 712.

Weitz, *Medizinische Klinik* 1912, No. 26.

Géronne, *Berliner klinische Wochenschrift* 1912, No. 36.

serum (prepared by Merck) and have proclaimed the serum to be by no means harmless, is quite erroneous. If Géronne is unable to prove his statement by naming the authors, he will have to bear the reproach of having lightly put forward false statements. The fact that some authors have met with just as little success by the use of Merck's pneumococcus serum as by the use of pneumococcus serum from other sources, is to be expected from the nature of serum therapy, but cannot be advanced as a peculiarity of Merck's serum, especially as in the case of several of these authors the cause of failure is evident. Thus, von Dorendorf finds his unfavourable opinion on the results of 12 cases. Five of these were complicated by very unfavourable circumstances, i. e., 2 by old age (64 and 68 years), one by mitral insufficiency and stenosis, one by alcoholism and one by chronic nephritis. In the remaining cases Dorendorf observed "a marked fall of temperature of 1 to 2 degrees in seven cases, and an improvement in the subjective symptoms lasting for hours in seven patients". If Dorendorf considers that these few and in part exceptionally severe cases justify him in forming an unfavourable opinion, it must be noted that he generally used only 28 c. c. of serum, whereas other authors (Weitz and Géronne), who worked with Neufeld's serum, gave as much as 50 to 100 c. c. Thus, if the majority of Dorendorf's cases showed a fall in temperature and improvement in the subjective symptoms, it would seem probable that by the employment of larger doses and with more normal subjects, better results would have been obtained.

Thus Beltz, who treated 25 cases of pneumonia by means of Merck's pneumococcus serum, among which there were no exceptionally severe cases, found that the crisis occurred considerably earlier than in those cases not treated by serum. He did not meet with any harmful result\*) and he has come to the following conclusion: I therefore do not hesitate to recommend the intravenous injection of large doses of serum in all cases which come under treatment early, especially if for any reason it is desirable to cut short the pneumonic process as rapidly as possible.

In the case of a boy aged 12, who suffered from cerebro-spinal meningitis and exhibited pneumococci in the spinal fluid,

Dorendorf, Medizinische Klinik 1912, No. 39.

Beltz, Deutsche medizinische Wochenschrift 1912, No. 1.

\*) In opposition to Géronne's unproved statement.

J. H. Cumming, after withdrawing 10 c. c. of spinal fluid, injected 3·5 c. c. (100 I. U.) of pneumococcus serum Merck\*). The injection gave rise to considerable pain and a rise of temperature. On the two following days the same dose was repeated, whereupon the temperature fell and rose once more. After a further injection of 7 c. c. (200 I. U.) the headaches ceased, the head retraction improved and the legs could be straightened. Six further injections were therefore administered and led to the disappearance of the symptoms and to a cure.

### Streptococcus Serum Menzer.

A. Menzer discusses in an interesting paper his experiences with regard to the results obtained by the treatment of acute articular rheumatism with and without antipyresis. He has come to the conclusion that this disease represents a streptococcal infection carried by way of the respiratory passages and that its symptoms, such as inflammation of the joints and inflammation of the heart and serous membranes, represent healing reactions of the metastases formed at the beginning of the infection. No treatment is capable of preventing these reactive inflammations from arising and the only question is by means of which treatment complete cure may be most surely effected. These natural healing processes are disturbed by antipyretics such as salicylic preparations; they cannot remove the cause of the disease and only influence pain, inflammation and fever. By means of treatment without antipyresis, by application of local and general warmth, and if necessary by injections of streptococcus serum\*\*); considerably better results are obtained, as regards complete restoration and diminution of relapses, than by treatment by salicylates, etc.

### Syphilis Reaction of Noguchi (Luetin Reaction).

Various investigators, as for example Tedeschi, Meirowski, Ciuffo, Gautier and others, sought a simple

Cumming, Lancet 1912, 9<sup>th</sup> November.

\*) Compare Merck's Report 1909, p. 62.

Menzer, Zeitschrift für Hygiene und Infektionskrankheiten Vol. 68, 1911.

\*\*) Compare Merck's Report 1909, p. 17.

Tedeschi, Gazzetta degli ospedali e delle cliniche 1908, No. 59.

Meirowski, Archiv für Dermatologie, Vol. 94, No. 2.

Ciuffo, Gazzetta medica italiana 1909, No. 43.

Gautier, Comptes rendus de la société de biologie 1910, No. 6.

reaction for syphilis analogous to the cutaneous reaction of von Pirquet. But the tests were unsatisfactory, as the authors lacked a pure antigen, which is essential for a satisfactory syphilis reaction. Now Noguchi seems to have attained the desired result, as appears from his communications and from an experimental study by H. Kämmerer.

Noguchi prepared an extract from pure cultures of *spirochæta pallida*, by grinding up in a mortar ascites-agar nutrient media containing innumerable spirochetes and mixing with it a fluid ascites culture likewise very rich in spirochetes, until a thin emulsion was produced. This was sterilised at 60° C. and 0·5 p. c. carbolic acid added. The preparation thus obtained is named "Luetin" by the author. The experiments carried out with it on human beings, which consisted in administering subcutaneous injections of 0·05 c. c. into the patient's upper arm, showed that these injections always gave a positive local reaction in undoubtedly tertiary and hereditary syphilis, while in primary and secondary syphilis and in metasyphilitic affections a positive reaction was obtained in comparatively few cases. According to Noguchi, 3 stages of the reaction may be distinguished: 1. Papular form, distinguished by a large, distinct, hard papule, 5 to 10 cm. in diameter, between 24 and 48 hours. The papule is surrounded by a diffuse red zone. The induration increases during the following 3 to 4 days, then the reaction disappears (with exceptions) gradually in the course of a week. 2. Pustular form, consisting of a papule as described under 1., which becomes oedematous from the 4<sup>th</sup> or 5<sup>th</sup> day on, while the inflammation continues and multiple, miliary vesicles are formed; 24 hours later it is transformed into a blister, containing at first clear and later purulent matter. The blister usually opens spontaneously and this is followed by the formation of crusts and gradual retrogressive changes. 3. Torpid form, distinguished by its delayed appearance.

G. Nobl and K. Fluss, who carried out confirmatory tests of Noguchi's syphilis reaction, were unable to form a definite opinion as to the value of this method, while Kämmerer does not, on the whole, criticise it unfavour-

Noguchi, Journal of Experimental Medicine 1911, Vol. 14, No. 6.

— Münchener medizinische Wochenschrift 1911, No. 45.

Nobl-Fluss, Wiener klinische Wochenschrift 1912, No. 13.

Kämmerer, Münchener medizinische Wochenschrift 1912, No. 28.

ably. Above all he found that the reaction is neither dangerous nor especially trying for the patient. It is specific for syphilis, but it is not always easy to interpret the result with certainty. On account of the slow course of the torpid form, a fortnight's time should be allowed in apparently negative cases. Although more than half of the cases of syphilis tested gave a negative reaction, Kämmerer believes that the reaction promises to form a useful supplement to the complement deviation test, and on account of the simplicity of the method is perhaps destined to supply the general practitioner with a valuable means of diagnosis. J. M. Wolfsohn and R. B. H. Gradwohl also attach a certain amount of value to the test.

#### Tetanus Antitoxin.

Besides the dry tetanus antitoxin of Tizzoni described in my Annual Report of 1909, I now also supply a liquid tetanus antitoxin of Tizzoni, the prophylactic dose of which consists of 5 to 10 c. c. (corresponding to 200 000 I. U.), and the curative dose of 25 c. c. (corresponding to 1 000 000 or 1 500 000 I. U.). I have also added to my list the curative tetanus antitoxin of Behring, which is under state control; this is also put on the market in a solid and liquid form. 20 A. U. of this are injected subcutaneously for prophylactic purposes. For curative purposes 100 A. U. are injected and the injection repeated after 24 hours if no retrogression of the tetanic symptoms is observed. In unusually severe cases the antitoxin may be given by intralumbar injection, but for this purpose a freshly prepared solution of the solid antitoxin is used, as the liquid contains a certain amount of carbolic acid. Further notes will be found in the directions accompanying each package.

Several communications on the therapeutic employment of tetanus antitoxin have been made by E. v. Graff, Young,

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Wolfsohn, Bulletin of the Johns Hopkins Hospital 1912, Vol. 23,  
p. 223.

Gradwohl, Medical Record 1912, No. 21. — Klinisch-therapeutische  
Wochenschrift 1912, No. 50.

v. Graff, Mitteilungen aus den Grenzgebieten der Medizin und Chi-  
rurgie 1912, Vol. 25, p. 145.

Young, Journal of the American Medical Association 1912, Vol. 58,  
No. 8.

Ch. Achard, Semple and F. Schweizer. Schweizer reports upon the treatment and cure of a child weighing 3 kilogrammes, who was taken ill on the 8<sup>th</sup> day and came under treatment on the 12<sup>th</sup> day; and Semple reports upon the value of the antitoxin in tetanus infections due to injections of quinine. The author attributes these infections not to faulty technique of the injections nor to an unsatisfactory condition of the injection fluid, but to the fact that the quinine injections may give rise to tissue necrosis, which provides an area of diminished resistance for the tetanus germs. Achard describes a case of a man, to whom he gave an intravenous injection of tetanus antitoxin 12 days after infection, which was followed by a cure in a short time without further therapeutic measures. Young also obtained very good results by the use of large doses of tetanus antitoxin in several cases in which the prognosis was exceedingly bad. He is of opinion that the antitoxin should be given in larger doses than has hitherto been the case. v. Graff is in favour of intravenous injection, as in opposition to previous views he believes it to be more efficacious than either subcutaneous or intramuscular injection. He demonstrated in animals that by intravenous injection an infection with several times the lethal amount could be neutralised and rendered innocuous.

### Tuberculol.

As the result of extensive experiments, von Holten has expressed a highly favourable opinion with regard to tuberculol, an opinion which, as is also admitted by Sell, justifies further investigation and employment of this remedy. As I have previously reported upon the preparation and the composition and value of tuberculol, I shall confine myself to a description of von Holten's results\*).

von Holten resorted to the use of tuberculol after a number of failures attending the use of old tuberculin and bacillary

Achard, Bulletin de la société médicale des hôpitaux de Paris 1912,  
p. 184.

Semple, Scientific Memoirs of the Government of India 1911, No. 43.  
Schweizer, Revista de la sociedad medica Argentina 1911, No. 109.  
Holten, Verhandlungen der Vereinigung der Lungenheilanstaltsärzte  
auf der 7. Versammlung zu Hamburg, June 1912, IV. Suppl. Vol.  
of the Beiträge zur Klinik der Tuberkulose.

\*) Compare Merck's Reports 1899, 1900, 1906, 1909 and 1910.

emulsion. In order to test the preparation and to establish its therapeutic value as surely as possible, the author only used it at first in severe cases in the third stage, in which numerous consonating râles were present and in which tubercle bacilli were found in the sputum. In 23 patients of this kind the improvement was the greater the higher were the doses of tuberculol it had been possible to inject. In 5 cases a final dose of 0·1 gramm of tuberculol was reached. The result in these 5 cases was better than any met with by the author among many hundreds of cases, with only a few exceptions. All the patients were, at the beginning of treatment, suffering from a severe pulmonary condition and had tubercle bacilli in the sputum; after 16 to 20 weeks' treatment the bacilli had in every case disappeared from the sputum and no râles could be detected, except that in 2 patients a few dry râles were heard over isolated patches. The author obtained these noteworthy results by the use of tuberculol B. He states that tuberculol A also furnishes good results, but is less efficacious than tuberculol B. Certainly cases treated with tuberculol C were less benefited than those treated with tuberculol B. The author draws the conclusion that the principal action which promotes cure is due to the endotoxins, the bacillary extracts.

In very severe cases in which cavities were present, the author obtained less satisfactory results during the time at his disposal. He attributes this to the fact that in many cases, and especially in severe ones, a longer period of treatment is required. As was pointed out by Landmann, the patients should not merely be endowed with a slight degree of immunity by injecting increasing doses of tuberculol and the treatment then discontinued; rather the patients should be worked up to the highest possible degree of immunity and should be kept there as long as possible, as they are only able to resist the specific bacilli when the immunity has attained a certain height. In the author's experience, a course of treatment lasting at least 6 to 12 months is required, even though the curative effect of tuberculol treatment becomes evident much sooner, after only 4 months.

In one case von Holten met with a prolonged high temperature after the administration of his smallest dose of tuberculol ( $5/1000000$  of the lethal dose). Even though occurrences of this kind cannot be absolutely avoided, yet the case shows that it may be necessary to begin with still smaller doses.

Thus, in order to retain or to increase the degree of immunity conferred during institutional treatment, the author considers that in severe cases tuberculol treatment should be continued by the private practitioner, who should be informed by the institution of the date and the amount of the last dose.

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### Sida Rhombifolia.

The variety *Sida* L. constitutes a subdivision of the Malvaceæ, comprising about 70 species, almost all of which are indigenous to Central America. Synonymous with *Sida* are *Dictyocarpus* Wight, *Malvella* Jaub. and *Fleischeria* Steud. *Sida rhombifolia*, a member of this family fairly widely distributed in the Tropics, has long been recognised as an internal remedy for pulmonary tuberculosis and rheumatism, and as an external remedy for snake-bite. The root of *Sida* has also been used as a substitute for the root of marshmallow, and as a mucilage. Its use as a curative remedy probably originated with the Indians. The constituent of the plant to which its therapeutic action may be attributed must be left to be decided by chemical investigation.

Fresh interest has recently been shown for *Sida* under the name of Mesbé, which is possibly of Indian origin; G. Heermann has carried out experiments with *Sida* extract in tuberculosis, which confirm the value of the plant in this disease. The author reports upon 3 cases of local tuberculosis, some of them accompanied by deep-seated ulcerative disintegration, in which local application (inhalation) proved highly beneficial. Heermann does not report upon the preparation, concentration and exact method of application of mesbé extract. Therefore, further communications from the author or from others must be awaited, especially as the few cases reported furnish insufficient proof, and a scientific foundation for *Sida* therapy is wanting. A. Spangenberg has attempted to furnish this. He attributes the expectorant action of mesbé extract or of the drug itself to the ammonia salts it contains, its action in improving the appetite to the bitter principles and

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Heermann, Münchener medizinische Wochenschrift 1912, No. 34,  
p. 1849.

Spangenberg, Reichs-Medizinalanzeiger 1912, p. 545.

essential oils, its action in digestive disorders to sulphates, and the astringent action in haemoptysis to tannic acid. In his experience, the preparation gives very good results in the local treatment of lupus and tuberculosis. It also furnishes good results in the form of drinking cures and inhalations in pulmonary tuberculosis, without giving rise to any harmful secondary effects. There is said to be marked improvement in the expectoration, the cough and the night sweats.

The results of Zink's investigations are not in agreement with the favourable opinion expressed by the above named authors; he treated a number of cases without success. He considers that mesbé extract does not exert any specific action upon tuberculosis. The author was only able to establish a certain antiseptic action, which did not suffice to proclaim the preparation a curative remedy in tuberculosis.

### Silicic Acid, Preparations of

The salts and esters of silicic acid have gained considerably in interest on account of the publications of A. Zeller; the soluble alkaline silicates especially may be expected to play an important part in future in the treatment of cancer. The author has published the results of several years' experiments, which show without doubt that sodium silicate and potassium silicate are of considerable assistance in the treatment of sarcomata. Zeller also carried out experiments with esters of silicic acid, but did not state which ester he used. It may be assumed that they did not give the desired results, as he finally restricted himself to medication with sodium and potassium silicate.

Zeller's cancer treatment, which is at present only applied to carcinomata accessible from the exterior, consists in the internal administration of alkaline silicates and the external application of a mercury and arsenic paste. His prescription reads:

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Zink, Münchener medizinische Wochenschrift 1912, No. 50, p. 2732.

Zeller, Münchener medizinische Wochenschrift 1912, No. 34, p. 1841,

No. 35, p. 1916 and 1936, No. 38, p. 2088. (Compare C.

Lewin, Therapie der Gegenwart 1912, No. 9, p. 403 and S. Schick,

Wiener medizinische Wochenschrift 1912, No. 48 and 49.)

For the history of Zeller's method of treatment of cancer see

J. Wolff, Deutsche medizinische Wochenschrift 1912, No. 38, p. 1789.

Rp. Potassii silicici	20.0	grammes	( $\frac{2}{3}$ oz)
Sodii silicici	20.0	„	( $\frac{2}{3}$ „)
Sacchar. lactis	60.0	„	(2 „)
M. Sig.: 0.25 gramme (4 grains) to be taken 3 times a day.			

Rp. Acid. arsenios.	2.0	grammes	(30 grains)
Hydrarg. sulph. rubr.	6.0	„	(90 „ )
Carb. animalis	2.0	„	(30 „ )
M. Sig.: The powder to be mixed with water and used as a cancer paste.			

The author named the silicate mixture "Nacasilicium", the paste "Cinnabarsana". They are used as follows:

The cancerous tumour and the surrounding area are cleansed with cotton wool soaked with benzine and then the paste is spread on thickly. When it has dried, in small ulcers the paste is covered over with collodion, in larger ulcers it is covered over with an 8-fold layer of gauze and with cotton wool, and the dressing is fixed with a suitable plaster. The paste treatment is repeated every 8 to 14 days, according to its effect. At the same time 0.25 gramme (4 grains) of the silicate mixture in a little water is given 3 times a day. The internal medication is continued for at least a year after the paste treatment has been left off, even if healing has been effected; this can readily be carried out, as the silicate mixture is usually well tolerated. It goes without saying that only pure potassium and sodium silicate must be used for the preparation of the silicate mixture. The appetite and the digestion are, according to Zeller, very well regulated by means of this medication. With regard to secondary symptoms caused by the paste, in his experience no pains arise in dealing with small ulcers, but in larger cancers pains arise which are often severe and may continue for many days. The cancerous ulcer may sometimes increase to double its size at first and then forms a chocolate coloured, spongy swelling. The paste does not attack normal tissue so strongly, but if it should cause necrosis, it assumes a yellow, dirty colour. As soon as the cancerous ulcer has died away, an ulcer remains having a dirty yellow base; it is soon cleansed by treatment with benzine and salicylic-zinc ointment and then heals completely. The cosmetic result is said to be excellent.

Of 57 cases suitable for this treatment, Zeller cured 44 in the course of about 9 months, while 10 are still under treatment. Three of his patients died. The result is therefore highly favourable.

As the alkaline salts of silicic acid are strongly hygroscopic, the mixture prepared according to Zeller's instructions easily cakes and may become yellow or brownish on account of the alkalinity of the silicates. Meubrink therefore suggests that a little magnesia be added to the mixture. The prescription would then read as follows:

Rp. Sodii silicici	20.0	grammes	( $\frac{2}{3}$ oz)
Potassii silicici	20.0	„	( $\frac{2}{3}$ „)
Magnes. lev.	20.0	„	( $\frac{2}{3}$ „)
Sacch. lactis	40.0	„	( $1\frac{1}{3}$ „)

M. Ft. pulv. D. ad vitr.

If the mixture is to be given in water, it is advisable to prescribe a mixture of equal parts of potassium and sodium silicate in suitable doses.

Ladendorf draws attention to the utility of silicic acid in pulmonary tuberculosis, administered in mineral water (Compare Merck's Report 1906, p. 234); he obtained very good results by means of this treatment.

### Silver, Colloid

Colloid silver, according to Gennerich, is deserving of special consideration in gonorrhœal rheumatism and in other acute complications of gonorrhœa. According to the author, colloid silver, or collargol, should be applied intravenously as early as possible, so long as the presence of inflammatory symptoms indicates the persistence of virulent pathogenic organisms. In quite recent cases, collargol treatment is sufficient by itself to bring about complete recovery in a short time. The author's technique is as follows:

A 1 p. c. solution of collargol, or of colloid silver, is used, which is freshly prepared daily and is sterilised by heating in boiling water. A towel is tied tightly round the upper arm, so that the radial pulse can just be felt. After clenching

Meubrink, Medizinische Klinik 1912, No. 39, p. 1609.

Ladendorf, Zeitschrift für Balneologie 1912, No. 6.

Gennerich, Münchener medizinische Wochenschrift 1912, No. 15, p. 811.

the fist vigorously several times, the cutaneous veins become distended and prominent. When the vein is punctured with the half-filled Record syringe (20 c. c. capacity) the piston immediately rises, whereupon the tight band is at once removed from the arm. The dose of 10 c. c. must be administered in the space of 2 to 3 minutes. The largest single dose which Gennerich prescribed was 15 c. c. of the 1 p. c. solution, but it places too great a strain upon the organism; though it might otherwise be indicated on account of its greater efficacy. As the desired result cannot be attained by a single injection, the author is in favour of continued treatment with doses which are non-injurious to the organism. Accordingly, injections of 8 to 10 c. c. must be continued and repeated daily, not only until the fever has remained absent for several days, but until local examination shows that the pathogenic organisms have been destroyed. In small and weakly persons a single dose of 6 to 7 c. c. will be sufficient. Should the patient feel unwell after several applications of collargol, the treatment must be discontinued. If in badly neglected cases suppuration and abscess formation occur, or if, when the process is completely at an end, no improvement in the articular functions can be expected, operative measures are adopted.

Collargol is also useful in diseases of the bladder, in which injections of 100 c. c. of a 0·5 to 1 p. c. solution prove beneficial in all cases, unless mixed infection is present. All recent inflammations of the testicle and epididymis, according to Gennerich, form indications for collargol treatment. In these cases, intravenous injections always bring about a rapid fall of temperature and a diminution in the local swelling, as well as improvement in the general health.

J. K. Stonkuss confirmed the favourable influence of collargol on syphilis in 22 cases, which he had treated by intravenous injections. In primary syphilis, the symptoms disappeared after 1 to 5 injections of 5 to 10 c. c. of a 2 p. c. solution of collargol.

E. Braendle, induced by Gennerich's communications, prescribed electrargol and fulmargin with satisfactory results in gonorrhœal arthritis and epididymitis. His observations embrace 56 cases of epididymitis and 17 cases of gonorrhœal

arthritis. Intramuscular injection has proved the most acceptable method of application, but the two preparations may also be injected subcutaneously or locally. In gonorrhœal rheumatism he injected 10 c. c. of electrargol every 2 or 3 days as required. The injections were well tolerated and were painless. With the same dosage, good results were obtained in epididymitis. In obstinate cases, the injection may be made into the substance of the epididymis (dose 1 c. c.).

Engelen also used fulmargin with benefit in erysipelas.

According to W. Kausch, collargol injection yields excellent results in septic processes. Intravenous application of collargol removes septic fever with its secondary symptoms. It is also efficacious in pyæmic processes, in which the temperature remains raised even after the focus of suppuration has been opened up. The usual dose for adults is 10 to 25 c. c. of the 2 p. c. solution, according to the severity and duration of the case; with due precautions and slow injection as much as 100 c. c. may be given. The author fixes at least 3 minutes as the duration of an injection of 10 c. c., 10 minutes for 50 c. c., and 15 minutes for 100 c. c. In carcinomata he has also injected doses up to 100 c. c. In these the drug calls forth a typical, striking general and local reaction, but the author is as yet unable to say whether it effects a cure.

Intravenous injection of collargol is also recommended by Fehde. If the severe general reactions sometimes occurring after this method of application are feared, they may be avoided by first injecting a small dose, of about 0·05 grammie ( $\frac{3}{4}$  grain) of collargol, after which larger doses will not call forth a reaction. After the injection of the amount mentioned, increasing amounts are injected, up to 0·2 to 0·25 grammie (3—4 grains), for it is practically certain that a single injection will be without effect in severe sepsis. The author found this treatment very valuable in puerperal infections. But, in his experience, it should be used as a prophylactic in confinements, 0·1 to 0·15 grammie ( $1\frac{1}{2}$ — $2\frac{1}{3}$  grains) being injected on alternate days. The author describes the technique in detail. Apart from gynæcological cases, intravenous injection of collargol

is beneficial in typhoid fever, angina, rheumatic affections and endocarditis, and in mixed infections of tuberculosis.

In many cases of sepsis, rectal application may be substituted for intravenous injection. According to E. v. Meyer, the patient is first given a rectal wash-out, a quarter of an hour later the rectum is irrigated with a copious supply of a 1 p. c. solution of sodium chloride or soda, in order to remove any mucus present in the rectum and sigmoid colon, and 15 minutes later the collargol is injected. In severe acute cases, 50 to 100 c. c. of a 5 p. c. solution in lukewarm water are used, and in milder, acute cases the same quantity of a 2 to 3 p. c. solution. In mild, chronic cases 1 gramme (15 grains) is sufficient at first, and later 5 grammes (75 grains) of collargol to an enema. It is applied twice a day, and after improvement has taken place, once a day, and is continued for at least 8 to 14 days. If the enemata are not well retained, 8 to 10 drops of tincture of opium are added, or the daily dose of collargol may be divided and given in 4 to 6 enemata.

### Sodium Bicarbonate.

Labbé, Bith and Fertyk have found sodium bicarbonate to be useful especially in diabetics\*) losing weight. In these cases, large doses generally effect an increase in weight. O. Hansen made the same observation in diabetics who had received 20 to 30 grammes ( $\frac{2}{3}$ —1 oz) a day; but he found that after prolonged administration of the drug, the weight became constant, or even decreased. He considers the increase to be due to the retention of water. The length of time during which relief from coma can be obtained by injections of sodium bicarbonate is still an open question, for in one case the author brought about a cure by the intravenous application of 5 litres of a 4 p. c. solution; but after 2 months there was a recurrence with a fatal issue. Nor could the injection

v. Meyer, Allgemeine medizinische Zentralzeitung 1912, No. 26,  
p. 331.

Labbé, Bith, Fertyk, Revue internationale de médecine 1912, No. 12,  
p. 220.

\*) Compare Merck's Report 1911, p. 411.

Hansen, Zeitschrift für klinische Medizin 1912, Vol. 76, No. 3.

prevent death in other patients. On the other hand, albuminuria consequent upon acidosis was, as a rule, favourably influenced.

Binet offers various suggestions for the employment of sodium bicarbonate in gastric disorders. The symptoms caused by disturbances of motility are usually best treated by doses which are not too large. Daily doses of 5 to 6 grammes (75—90 grains) usually suffice. The drug should be avoided in gastric cancer and in gastric ulcer. The administration of a mixture of 0·8 gramme (12 grains) of sodium bicarbonate, 0·2 gramme (3 grains) of magnesia levis and 0·01 gramme ( $\frac{1}{6}$  grain) of *folia belladonnae* has proved beneficial. In pains due to dyspepsia this powder is given one hour, and again half an hour before meals, and half an hour and one hour after meals. If hypersecretion and spasm should occur, one powder is given every  $1\frac{1}{2}$  hours during the period of digestion. For pain, a solution of 8 grammes (120 grains) of sodium bicarbonate, 2 grammes (30 grains) of sodium phosphate, 2 grammes (30 grains) of sodium sulphate in one litre ( $33\frac{1}{3}$  oz) of water may be prescribed, 150 to 300 grammes (5—10 oz) of which should be taken at a time.

In septic processes, Vorschütz has found the administration of sodium bicarbonate to be beneficial. He prescribed a solution of 20 grammes ( $\frac{2}{3}$  oz) in Seltzer water to be drunk by the patient. He attributes the favourable results obtained by this treatment to the catalytic property of the alkali and the retention of water, which brings about the powerful turgescence of the tissue and its oedematous infiltration, besides considerably raising the blood pressure. According to the author's report, the patients felt exceedingly well.

B. Brand employed sodium bicarbonate externally in gout. He applied to the inflamed joints dressings thickly covered with a paste of sodium bicarbonate and water and kept continuously moist. The results are said to be surprisingly good.

### Sodium Cacodylate.

As a supplement to my former communications on this subject, reference may be made to the results of cacodylic acid

Binet, *Revue de thérapeutique* 1912, No. 14, p. 486.

Vorschütz, *Zentralblatt für Chirurgie* 1912, No. 50, p. 1719.

Brand, *Neerlandsch Tijdschrift voor Geneeskunde* 1912, p. 978.

therapy obtained by A. Robin, J. O. Elrod, Newmayer, L. J. Spivak, P. G. Heinemann and J. J. Moore.

Robin still attaches great value to sodium cacodylate in the treatment of pulmonary tuberculosis. Besides other drugs, which he prefers for the permanent or periodic treatment of this disease, he prescribes a series of injections of sodium cacodylate. He directs that the patient shall receive, at some time suitable to himself, a daily deep subcutaneous injection of 1 c.c. of a 5 p.c. solution. Elrod reports very satisfactory results of injections of sodium cacodylate in pellagra, as Spivak does in syphilis. According to them, the preparation is not toxic if it is always injected in a chemically pure form and in freshly prepared solution, even if it is given daily for weeks in doses of 0.3 to 0.36 grammes (5—6 grains). According to the author, it is best to begin with daily injections of 0.18 gramme (3 grains) and gradually to increase this dose according to the results obtained. This medication proved particularly effective in the preliminary stage of syphilis, but it is also beneficial in primary syphilis in the macular forms of roseola. It acts rather more slowly upon papular cutaneous processes, but is quite efficacious in suitable doses. The plaques on the mucous membrane and condylomata disappear very quickly, even in the absence of any other treatment. On the other hand, even large doses are without effect in adenopathy, hypertrophy of cerebral ganglia, rupia and tertiary lesions. There is always an improvement of the general health and of the appetite, and an increase in weight, which adds to the patients' confidence in the treatment. Mercury treatment may be combined with the injections of cacodylate.

Newmayer attempted to prove by means of pharmacological experiments that the cacodylates were chiefly useful in diseases caused by protozoa, and only secondarily in bacterial infections. The results of his investigations show that in infections by *staphylococcus aureus*, the life of the experimental animals

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Robin, Bulletin général de thérapeutique 1911, 30<sup>th</sup> December. —

Revue de thérapeutique 1912, No. 4, p. 130.

Elrod, Journal of the American Medical Association 1911, Vol. 57, p. 719.

Newmayer, Therapeutic Gazette 1911, August.

Spivak, Semaine médicale 1912, No. 18, p. 207.

Heinemann-Moore, Journal of Infectious Diseases 1912, Vol. 10, p. 294.

could be prolonged by 12 to 17 days by treatment with cacodylic acid, but that a cure could not be effected. According to Heinemann and Moore, sodium cacodylate was of no use in guinea-pigs infected with spotted fever.

### Sodium Iodide and Hydrogen Peroxide.

Last year I reported upon Pfannenstill's method of treating local infectious processes with sodium iodide and hydrogen peroxide. S. A. Pfannenstill enlarged his former communication by reports of further cases. Among these are 9 cases of laryngeal tuberculosis, which were cured, and 5 cases which were not cured. His communications on the value of the method for external lupus and tuberculosis, in lupus of the nasal mucous membrane, and local tuberculous infections show that the combined iodine-alkali-hydrogen peroxide treatment is deserving of further tests. R. Mandl tried it in a tuberculous subject, who had for 23 years suffered from suppurative middle-ear disease and who refused operation. He first introduced tincture of iodine into the middle-ear by means of cotton wool fixed to a probe and followed it up by the application of solution of hydrogen peroxide, which he then carefully removed. After several applications of these drugs, the cavity of the middle-ear closed over in a normal manner. Finally the author dried the middle-ear with glycerin, and within 6 weeks the ear had healed and the hearing had improved. This success induced the author to carry out experiments with a preparation, which he calls "Ulsanin" (hydro-iodo-borate) and which, according to his statement, gives off iodine and oxygen simultaneously on coming into contact with moisture. It is said to have proved beneficial in tuberculous granulations and sores, and in indolent putrid wounds.

According to G. Wüstmänn, the alkaline iodide by itself is a good remedy for tuberculosis of the mucous membranes of the upper air passages. But he considers the local application of solution of hydrogen peroxide to be of doubtful value, for according to Pfannenstill's case histories, the cases thus treated did not heal more quickly than the cases in the Rostock Clinic, which were cured by means of po-

Pfannenstill, Nordisches medizinisches Archiv 1912, Vol. 44, innere Med. No. 4, p. 1.

Mandl, Deutsche medizinische Wochenschrift 1912, No. 51, p. 2417.

Wüstmänn, Deutsche medizinische Wochenschrift 1912, No. 47, p. 2239.

tassium iodide alone. He recommends that the cases refractory to potassium iodide be treated by iodine and mercury combined.

### Sodium Salicylate and Salicylic Acid.

E. Levin carried out investigations on the absorption of sodium salicylate when applied in various ways, and he came to the conclusion that the rapidity of absorption after subcutaneous injection of the preparation was about the same as in other methods of employment. On the other hand, subcutaneous application does not, by a long way, attain the maximum concentration in the blood, such as can be brought about by other methods of administration, as for example by intramuscular injection or by absorption from the alimentary canal. The sodium salicylate also disappears more rapidly from the blood when given subcutaneously. After 10 hours it can no longer be demonstrated in the blood, while sodium salicylate is present in the blood 22 hours after intramuscular injection, and 32 hours after internal administration. At the end of this time it has disappeared without leaving a trace.

The action of sodium salicylate after rectal application is noteworthy. Volland obtained a successful result in eclampsia, which justifies further tests of his method. He injected 5 grammes (75 grains) of sodium salicylate with the result that copious perspiration ensued, which was followed by a cure. L. G. Heyn reports brilliant results of the rectal employment of salicylates in acute articular rheumatism. In a number of cases, in which internal medication was not tolerated, he administered daily doses of 5 to 12 grammes (75—180 grains) of sodium salicylate in starch enemata, to which he added a few drops of tincture of opium. E. Crouzel recommends the rectal administration of the following prescription if large doses are required:

Rp. Sod. salicyl. 16·0 grammes (240 grains)

Acac. gum. pulv. 4·0 „ (60 „ )

Lactis cocti ad 120 c. c. (4 oz)

One tablespoonful of this mixture represents 2 grammes (30 grains) of sodium salicylate.

Levin, Deutsche medizinische Wochenschrift 1912, No. 51, p. 2412.

Volland, Therapeutische Monatshefte 1912, p. 351.

Heyn, Wiener klinische Wochenschrift 1912, p. 894.

Crouzel, Répertoire de pharmacie 1911, p. 289.

For the cutaneous treatment of rheumatic affections, the following ointment is, according to Scharff, useful:

Rp. Acid. salicylic.	10·0	grammes	( $\frac{1}{3}$ oz)
Ol. terebinth.	10·0	„	( $\frac{1}{3}$ „)
Sulphur. præcip.	40·0	„	( $\frac{1}{3}$ „)
Terebinthin.	40·0	„	( $\frac{1}{3}$ „)

Each of the components of the ointment is in itself an antirheumatic remedy, which is said to account for the specific action of the ointment. The best action is obtained by applying the mixture to the affected parts and covering it with guttapercha tissue or with Billroth battist. The first application usually only causes slight burning, but repeated applications in chronic processes are not free from pain, though they are said to be more bearable than the rheumatic pains themselves. Both lumbago and cervical myositis, according to the author, regularly yield within the first 24 hours after the application of the dressing. The pains of arthritis deformans, sciatica and neuralgia are also, with few exceptions, cured and this takes place more quickly than after internal medication. The hyperæmia caused by the ointment and its analgesic properties offer a prospect of success in the treatment of tenosynovitis, contusions and distortions.

According to Ströll, salicylic acid is also useful in furuncles of the face. For this purpose the following mixture is prescribed:

Rp. Acid. salicylic.	2·0	grammes	(30 grains)
Mellis crudi	20·0	„	( $\frac{2}{3}$ oz)
Extract. arnic. flor.	10·0	„	( $\frac{1}{3}$ „)
Farinæ tritici q. s. ut f. unguis.			

The remedy is applied on boric lint every 24 hours. On renewing the dressing, the part is cleansed with cotton wool and carbolic lotion. The boils should not be expressed. Healing is effected by means of boric acid ointment.

N. Rh. Blegvad brings about anaesthesia of the tympanic membrane by a mixture of 1 gramme (15 grains) of cocaine hydrochloride, 1 gramme (15 grains) of salicylic acid, 2 grammes (40 min.) of alcohol and 20 drops of adrenalin. A tiny pledge

Scharff, Therapeutische Monatshefte 1912, No. 2, p. 117.

Ströll, Münchener medizinische Wochenschrift 1912, No. 12, p. 675.

Blegvad, Deutsche medizinische Wochenschrift 1912, No. 28, p. 1337.

of wool is soaked in this mixture and is applied to the tympanum at the point to be incised. The burning sensation which immediately ensues soon disappears, and after 20 minutes anaesthesia has, as a rule, been induced. If this is not the case, the application must be repeated for 10 minutes more. If there are no perforations, anaesthesia can be hastened and strengthened by instilling about 10 drops of salicylate-cocaine solution into the ear after the pledget has been introduced, and closing the canal with cotton wool. This effects complete anaesthesia in the majority of cases after 10 to 15 minutes.

### Sodium Subphosphate.

The sodium salt of subphosphoric acid ( $\text{Na}_2\text{H}_2\text{P}_2\text{O}_6 - 4\text{H}_2\text{O}$ ) is, according to M. Koss, a suitable test for the demonstration of thorium in an acid solution. His experiments showed not only that thorium subphosphate is insoluble in concentrated acids, as had been stated by Kauffmann, but that all cerium and yttrium earths in acid solution form soluble salts of subphosphoric acid. On precipitation of thorium subphosphate none of these salts pass into the precipitate. To carry out the test, the solution to be tested is rendered strongly acid by hydrochloric acid, and a few drops of sodium subphosphate solution are added. In the presence of an appreciable amount of thorium, a white flocculent precipitate immediately separates. If only minute quantities are present, the reaction can be hastened by heating. The precipitate, according to Koss, has the following composition:  $\text{Th}(\text{PO}_3)_2 + 11\text{H}_2\text{O}$ . In the presence of 6 p. c. of hydrochloric acid, the reaction takes place if there is only 0.01 p. c. of thorium in the solution. In the presence of titanium and zirconium, which are also precipitated by sodium subphosphate, the test must be somewhat modified. Titanium is oxidised by hydrogen peroxide and is then not precipitated by the subphosphate. Zirconium is carried down in the precipitate, which, after having been oxidised by sulphuric and nitric acid, is brought into solution. This solution is treated with oxalic acid, whereupon the zirconium remains in solution and thorium is precipitated in the form of oxalate.

Koss, Chemiker-Zeitung 1912, p. 686.  
Kauffmann, Dissertation Rostock 1899.

The test has been further elaborated by A. Rosenheim for the analysis of Monazite sand.

### Sodium Taurocholate.

D. Danielopolu has elaborated a method for the diagnosis of meningitis, which depends upon the fact that in meningitis the cerebro-spinal fluid contains an increased amount of a substance which is capable of checking the haemolysis caused by sodium taurocholate. The author has not yet discovered which substance in the normal and the pathological cerebro-spinal fluid possesses this property.

The technique described by the author is as follows: A 1 p. c. solution of sodium taurocholate (Merck) in normal saline solution (0·95:100) is prepared. Its haemolytic strength is tested against a 2 p. c. suspension of dog's blood corpuscles (free from serum) in normal saline solution. The minimum dose of taurocholate solution is found which will cause complete haemolysis of 1 c. c. of the blood suspension in 30 minutes. Using Merck's sodium taurocholate, this dose was 0·2 c. c. of the 1 p. c. solution. The minimum doses used by the author in his experiments were 0·2 and 0·25 c. c. The cerebro-spinal fluid is centrifugalised for 15 minutes and is used as fresh as possible. For every pathological cerebro-spinal fluid 4 mixtures are prepared; two with 0·2 c. c. and two with 0·25 c. c. of taurocholate solution, while the dose of the cerebro-spinal fluid varies from 0·4 to 0·6 c. c. The amount of blood cells remains the same for all 4 experiments, i. e., 1 c. c. A further series of 4 mixtures contain the same amounts of taurocholate solution, blood cells and normal cerebro-spinal fluid of a healthy individual. Finally two little tubes of 0·2 and 0·25 c. c. of taurocholate solution and 1 c. c. of suspension of blood cells are prepared without the addition of cerebro-spinal fluid. All the mixtures are made up to 5 c. c. with normal saline solution and are kept in an incubator at 37° C. Every 5 minutes note is taken of the commencing or progressing haemolysis. It commences soonest in the tubes which do not contain cerebro-spinal fluid and last in those containing pathological cerebro-spinal fluid. The reaction may be regarded as finished as soon as

the tubes without cerebro-spinal fluid or with normal cerebro-spinal fluid show complete haemolysis. At this moment the tubes containing pathological fluid show no haemolysis or only very slight haemolysis.

The reaction described was, according to the author, positive in all cases of meningitis, even at the beginning of the disease, and when the cytological examination gave insufficient evidence for diagnosis. In cases of meningism it was always negative, as it was in individuals who, during the course of their disease, (infectious or not) had shown abnormal leucocyte reaction without any clinical symptoms of meningitis.

The reaction is of special practical significance: a) At the commencement of certain cases of meningitis, in which the leucocyte reaction is absent or is so slight that the presence of meningitis cannot be assumed. b) In meningism, as the absence of the leucocyte reaction is insufficient to eliminate a diagnosis of meningitis. The reaction does not give a clue to the type of meningitis.

St. Rosenblat found sodium taurocholate to have a strong bactericidal action on trypanosomes *in vitro*, but *in vivo* it failed, so that the finding is without significance for the treatment of trypanosomiasis.

G. Singer and K. Glaessner have published an interesting paper on the value of bile salts in constipation. According to them, taurocholic acid acts most promptly. Next to it comes cholic acid ( $C_{24}H_{40}O_5$ ), then glycocholic acid, while taurin and glycocoll proved ineffective. In practice, the sodium salts of these bile acids come into consideration. They act best on rectal application, as they take effect in the large intestine. If they are given internally, they must be enclosed in capsules which are not dissolved until they reach the intestine. The authors administered cholic acid in doses of 0.3 to 0.5 gramme (5— $7\frac{1}{2}$  grains) in the form of suppositories, which caused the bowels to act in 10 to 30 minutes. Still more effective is the employment of sodium cholate in the form of enemata. It is therefore best to give bile acids or their sodium salts in the

Rosenblat, Archiv für Anatomie und Physiologie 1912, p. 188.

Singer-Glaessner, Archiv für Verdauungskrankheiten mit Einschluß der Stoffwechselpathologie und der Diätetik. 1912, Vol. 18, No. 2, p. 192. — Compare Merck's Report 1910, p. 345.

form of micro-enemata or macro-enemata, which are very useful in chronic constipation.

### Sodium Thiosulphate.

M. Oppenheim has for some years used a very simple method of treatment for pityriasis versicolor, which has not failed in a single case, even when other methods of treatment had previously proved unsuccessful. He used a 10 p. c. aqueous solution of sodium thiosulphate. It is used as a lotion for the affected areas of the skin and is applied at least 3 times daily. The diseased parts are lightly washed and rubbed with a cloth dipped into the solution, and are then dried. By means of this treatment the pityriasis areas grow pale in the course of 8 to 14 days and gradually disappear. Recurrences can be prevented by one application a day. The simultaneous use of alcohol has not, in the author's experience, proved beneficial. The treatment furnishes equally favourable results in erythrasma, but is less satisfactory in herpes tonsurans and pityriasis rosea.

Sabbatani recommends sodium thiosulphate to supplement disinfection of the skin by tincture of iodine. According to his instructions, the tincture of iodine is painted on in the usual way, the area is then covered with cotton wool, and after 5 to 10 minutes a lukewarm, aqueous, sterile 5 p. c. solution of sodium thiosulphate is poured over it. In this way the skin is disinfected and decolorised, and neither the surgeon nor the patient is particularly troubled by the smell of the iodine. Lemaire and Chabanier have sought to alleviate the local irritative effect of tincture of iodine by sodium thiosulphate solution. According to Taphanel, sodium bisulphite solution may be used in its place, for, in the author's opinion, it not only abolishes the secondary effects of iodine and removes the iodine stains from the skin,

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Oppenheim, Zentralblatt für die gesamte Therapie 1912, No. 9, p. 449.

Sabbatani, Gazzetta degli ospedali e delle cliniche 1912, No. 53.

Lemaire, Gazette hebdomadaire des sciences médicales 1912, 28<sup>th</sup> July. — Revue internationale de médecine 1912, No. 18, p. 323.

Chabanier, Presse médicale 1912, No. 65, p. 668.

Taphanel, Comptes rendus de l'académie des sciences 1912, No. 26, p. 1828.

but itself acts as a powerful disinfectant. Sabbatani, however, prefers sodium thiosulphate.

### Soft Soap.

More than 30 years ago Kappesser drew attention in a work published by Waitz in Darmstadt to the value of the soft soap treatment of scrofulous and tuberculous symptoms; and this method of treatment has, with time, gained somewhat in favour. Recently, the author has reported upon two further cases which throw a favourable light on Kappesser's method. One case was that of a child in the first year of life which, after having recovered from a severe affection of the bowels, was troubled with enormous swellings of the glands. By repeated cleansing with soft soap the trouble was removed in the course of 6 to 8 weeks, and there was no longer any apprehension of abscess formation. The same child, when 10 years old, was, by means of rubbing with soft soap, completely cured from an attack of conjunctivitis without any permanent injury being produced. At first little heed had been paid to the attack, but it had developed into keratitis of both eyes with severe photophobia. The other case was that of a man suffering from extensive ulceration of the face, with purulent discharge, probably a severe case of sycosis, which had not been improved by a course of treatment by X rays extending over 6 weeks. Soft soap was rubbed into the anterior surface of the chest and abdomen; improvement was observed after the first application, the profuse suppuration subsiding. Dry crusts were formed which, on coming away, left a healthy skin.

The action of soft soap has hitherto been explained by assuming that its absorption gradually improved the condition of the blood and lymph, the fat being directly conveyed to the blood and lymph channels. Others (like Kollmann) sought the explanation in the penetration of potassium into the blood. Kappesser does not agree with these hypotheses, as such surprisingly rapid cures or improvement of such severe pathological symptoms as those recorded above cannot be due to the gradual improvement of the composition of the blood. He therefore considers it a worthy problem for pharmacology to explain the action of soft soap by experimental means.

In consequence of the good results obtained by Kappesser, B. Mosberg has recommended a preparation named "Sudian" for the treatment of scrofula and surgical tuberculosis; it consists of 3 parts of sulphur, 17 parts of saponin and 80 parts of soft soap and is standardised to contain 0·4 p. c. of alkali. It is said to possess the advantage over soft soap of not irritating the skin. Kappesser asserts that ordinary soft soap answers all requirements in carrying out his treatment, and that its substitutes, such as sudian, can be dispensed with.

### Sophol.

In order to decide which of the silver salts at present in use was most efficacious in the prophylaxis of ophthalmia neonatorum, A. Lehle carried out experiments at the University Hospital for Women in Munich with silver nitrate, silver acetate, and sophol\*). He came to the conclusion that sophol was preferable on account of its bactericidal power, its absolute painlessness and the almost complete absence of irritation. He also concluded that on account of its freedom from danger and of the fact that it will keep for months, its employment may be left to lay hands.

Lehle used a 5 p. c. sophol solution in 2500 cases. Irritative symptoms occurred in only 8 p. c. of his cases, and of these 6 p. c. suffered merely from epiphora, 1·5 p. c. from slight redness, slight swelling with turbid serous secretion, and 0·5 p. c. from purulent conjunctivitis. Thus in 92 p. c. of the children no irritative symptoms were observed.

The investigations of J. Fr. Unterstenhöfer also gave results in favour of sophol. The question as to whether sophol represents an ideal prophylactic must, in the author's opinion, be answered in the negative, because its solution does not keep well. But, in agreement with v. Herff, he found that sophol solutions which have undergone decomposition merely give rise to harmless catarrh of the conjunctiva or to no reaction.

J. F. Moran reports equally favourable results of sophol prophylaxis.

Mosberg, Fortschritte der Medizin 1911, No. 32.

Lehle, Münchener medizinische Wochenschrift 1912, No. 40, p. 2161.

Unterstenhöfer, Münchener medizinische Wochenschrift 1912, No. 43, p. 2361.

Moran, Washington Medical Annals 1912, No. 4.

### Sparteine.

The value of sparteine sulphate as a cardiac drug has been re-tested by Julien. His results may serve as a supplement to my references to sparteine and to its therapeutic employment\*). The author administered the alkaloid several times a day in doses of 0.02 to 0.03 grammes ( $\frac{1}{3}$ — $\frac{1}{2}$  grain), which give rise to no danger of poisoning\*\*), but only take effect slowly, i. e., in the course of 1 to 2 hours. The action lasts for about a day. It consists in a rise in the blood pressure and the strengthening of the cardiac action, but is manifested differently in healthy and sick subjects. In healthy subjects sparteine hastens the cardiac action, while in cases of heart disease it regulates the action, diminishing pathological tachycardia and hastening the action in bradycardia. It is therefore useful in acute affections of the myocardium with cardiac debility, especially in typhoid fever, and should also prove useful in nephritis. It also comes into consideration in circulatory disturbances due to fat embolism, and especially in chloroform anaesthesia. But on account of its slow action it is of little use in urgent cases and can never form a substitute for an intravenous injection of strophanthin.

Deléarde also regards sparteine sulphate as a good remedy in the treatment of typhoid, especially for children. He prescribes it alone or combined with strychnine sulphate, giving 0.02 gramme ( $\frac{1}{3}$  grain) of sparteine sulphate to children under 5 years of age, and 0.05 gramme ( $\frac{3}{4}$  grain) to children over 5 years old by subcutaneous injection in the course of 24 hours, according to the following prescription:

Rp. Spartein. sulph.	0.5 gramme ( $7\frac{1}{2}$ grains)
Strychnin. sulph.	0.005 gramme ( $\frac{1}{12}$ grain)
Aq. destill. steril.	10.0 grammes ( $\frac{1}{3}$ oz)

1 c. c. of this solution represents 0.05 gramme of sparteine sulphate and 0.5 milligramme of strychnine sulphate. For children under 5 years of age the strychnine should be omitted. Thus 1 c. c. of the solution is the daily dose for a child over 5 years old. In action it is equal to an injection of camphor.

Julien, Thèse de Bordeaux 1911.

\*) Compare Merck's Report 1911, p. 110—114.

\*\*) For the maximum dose of Sparteine compare Merck's Report 1911, p. 113.

Deléarde, Echo médical du Nord 1912, 18<sup>th</sup> August. — Revue internationale de médecine et de chirurgie 1912, No. 19, p. 338.

**Stained Tissue Nuclei for Testing Pancreatic Function.**

Under this designation I put on the market a preparation prepared according to the directions of A. Schmidt and T. Kashiwado, intended to be used for diagnostic purposes as a substitute for fragments of meat. The patient to be examined is given 2 capsules, each consisting of 0·25 grammes of mixed powder (equal parts of lycopodium and stained nuclei), either after the midday or the evening meal (on 2 consecutive days if necessary). Then the next stools are examined. Usually the powder can be demonstrated in the first faeces passed.

Part of the stain of the stained nuclei occasionally passes into the faeces, whether or not the nuclei have been digested. A stool of this kind, either in toto or only superficially, assumes a more or less blue colour, which becomes deeper on standing, or which may only appear then.

A portion of the stool the size of a nut is rubbed up in a mortar with a little water to form a thin emulsion. Then several, at least three, microscopic slides are prepared from it. If the stool is fluid, the slides may be prepared straight away. The preparations should be made from the more deeply stained parts. A dry lens is first used to search for lycopodium grains. Lycopodium is easily recognised. If it is present, the stools may be assumed to contain the nuclei, provided that these have not been digested. The nuclei sometimes lie singly and sometimes in groups, they retain their rounded form and deep blue colour, which is readily recognised under an oil immersion. In case of doubt, an immersion lens should always be used.

The presence of numerous bismuth crystals interferes with the finding of the nuclei, and the addition of iodine solution is sometimes equally disturbing, as it stains any starch granules which may be present a deep blue. The patient must not have ingested lycopodium grains forming a dusting powder for pills.

The reappearance of the nuclei depends upon the duration of passage as well as upon the pancreatic secretion; if they pass through the whole digestive canal too rapidly (within 5

Schmidt-Kashiwado, Zeitschrift für experimentelle Pathologie und Therapie, Vol. 8, p. 353. — Deutsche medizinische Wochenschrift 1911, p. 466 and 1912, p. 180.

hours), they pass into the stools in spite of the presence of active pancreatic juice. In the diagnostic employment of the test, this circumstance, to which Schmidt has repeatedly drawn attention, must be taken into consideration.

If the stained nuclei are not found in the faeces when the duration of passage has been sufficient (at least 6 hours), the pancreatic function may with certainty be considered normal.

If all or the greater part of the nuclei are retained, considerable disturbance of pancreatic secretion is undoubtedly present.

### Sterilized Gelatin.

It has long been of interest to know whether the internal or the subcutaneous employment of gelatin gives better therapeutic results. Some information on the subject is contained in a paper by E. Cmunt, who carried out detailed experiments with regard to the action of gelatin given by mouth, by enema and subcutaneously, on the viscosity of the blood. His experiments show plainly that although the internal administration of gelatin gives rise to increased viscosity, it takes place much more slowly and to a less degree than after subcutaneous injection. Thus, in one case, 200 c.c. a day of a 3 p. c. gelatin solution were taken for 10 days, with a resulting rise of 0·6 in the viscosity of the blood. But a single subcutaneous injection raised the viscosity by 1·4 in 24 hours. This result perhaps explains the fact, which has long been known, that an injection of gelatin arrests haemorrhage much more rapidly than does the internal administration of gelatin. The probable reason is that gelatin is absorbed more rapidly from the subcutaneous connective tissue and that it is absorbed unchanged, without coming under the influence of the digestive ferments.

The rectal administration of gelatin appears to be of less value for raising the viscosity of the blood and thus arresting haemorrhage, for the author arrived at negative results in his experiments.

Besides raising the viscosity, gelatin injection also raises blood pressure, but no definite influence on the pulse rate could be observed.

The undoubtedly favourable action of gelatin has recently again been discussed by Umber and R. von den Velden. Umber, like Cmunt, considers the subcutaneous employment to be the most efficacious method of application. Since the introduction of the germ-free Sterilized Gelatin for Injection "Merck", this is unattended by danger, for when carried out aseptically tetanus infection may be entirely excluded. If the contents of 1 or 2 tubes (40 c.c.) of this gelatin solution are injected subcutaneously into the thorax of an adult, and if possible into the anterior upper thoracic region of the side on which the haemorrhage is to be localised, then, according to Umber, a useful act has undoubtedly been performed. The injections are usually not quite free from pain and thus, to a certain extent, bring about the involuntary rest of the bleeding side. The injections are continued until the expectoration is free from blood.

According to v. d. Velden, gelatin, like horse serum and ox serum, possesses the capacity of increasing the content of globulin in the blood, which promotes the coagulability of the blood. The author considers that in therapy gelatin is preferable to serum, because gelatin injections have not as yet given rise to symptoms of anaphylaxis in human beings, whereas this is often the case with serum injections. Although the author has not yet completed the experiments upon which he is at present engaged, he feels justified in assuming that sensibilisation by gelatin, when followed by injections of serum, excludes the danger of anaphylaxis.

As Umber had come to the conclusion, by the unpractical methods then in use, that gelatin does not promote the coagulation of the blood, he has recently induced Schultz to carry out fresh experiments. The exact experiments of this observer to determine the coagulation time of the circulating blood in pulmonary haemorrhage before and after gelatin injections, led in a series of cases to positive results, and occasionally to surprisingly good results.

Stephan and E. I. Landa report upon cases from their practice. Stephan, in a typical case of melæna vera in a child,

Umber, Zeitschrift für ärztliche Fortbildung 1912, No. 20.

Velden, Therapeutitscheskoje Oboshrenie 1912, No. 15.

Schultz, communicated by Umber l. c.

Stephan, Deutsche medizinische Wochenschrift 1912, No. 5, p. 246.

Landa, Wratschebnaja Gazeta 1912, No. 45.

gave subcutaneous and intramuscular injections of 10 c. c. of 10 p. c. sterile gelatin solution 3 times on the first day of treatment, besides 60 c. c. of 5 p. c. gelatin-tea solution by mouth. On the second day, the child was given 2 injections and 70 c. c. of gelatin-tea. Threatened collapse and marked pallor of the skin on the second day were treated by the author with subcutaneous saline infusions. On the following day the stools only contained traces of blood. The child made good progress. This case, according to Stephan, is a typical case of melæna vera promptly healed by gelatin treatment.

Landa obtained good results in hæmophilia by injections of 20 to 40 c. c. of sterile gelatin solution.

As calcium salts have recently been used with success in a variety of diseases, especially in haemorrhage, haemorrhagic diatheses, exudative cutaneous affections, hay fever, bronchial asthma, rickets, osteomalacia and tetany, A. Müller and P. Saxsl sought an efficacious form for applying calcium chloride. The internal administration does not come into consideration, because it only leads to slow and insufficient absorption of the calcium, the intravenous application is, in the author's opinion, too dangerous, and the subcutaneous injection gives rise to severe irritative symptoms. In order to avoid these, the author tried the injection of calcium chloride together with a colloid substance, viz., gelatin. This combination proved of value. It is now prepared with Merck's sterilized gelatin and put on the market under the name of "Kalzine".

In experiments on animals the authors found that the subcutaneous injection of kalzine renders the blood more rapidly coagulable and checks exudations, while the calcium is slowly excreted in the stools.

For human beings, the authors prefer the intramuscular injection of kalzine, according to the method described by Schindler for joha. With the usual aseptic precautions, they injected 5 to 7 c. c. of gelatin solution containing 5 p. c. of calcium chloride into the gluteus medius near the hip-joint, at a point which must lie in or laterally to the sagittal plane which passes through the lateral end-point of the gluteal fold, and  $1\frac{1}{2}$  to 2 finger breadths below the iliac crest. These

Müller-Saxsl, Therapeutische Monatshefte 1912, No. 11, p. 777.  
Schindler, Münchener medizinische Wochenschrift 1912, No. 41,  
p. 2233.

injections were never injurious, and were only rarely followed by moderate pain lasting for some hours.

In a number of cases, comprising haemorrhages and haemorrhagic diatheses, the injection of kalzine has given excellent results. This treatment also gave very good results in a few cases of Graves's disease, and in a case of true bronchial asthma, while a few cases of asthma, in which pulmonary emphysema and bronchitis formed the chief symptoms, were not improved.

Kalzine is, according to the authors, always indicated when the administration of calcium salts by mouth is ineffectual, or when the severity of the condition calls for more effective measures. By means of kalzine injections the full effect of calcium is obtained in the organism, and the percentage of calcium is increased to an extent which cannot be effected by other methods. Besides the diseases mentioned above, it would therefore be worth while to try the preparation in exudative skin diseases, acute inflammations of the joints, bones, serous membranes and other internal organs, and in various irritative nervous conditions, such as occur in diabetes insipidus, tabes dorsalis, paralysis agitans, etc.

#### Sterilized Kaolin.

Vaginal treatment by powder is coming more and more into use, and the time is probably not distant when it will entirely supplant treatment by vaginal irrigation in many diseases, especially in leucorrhœa. M. Nassauer is an ardent advocate of kaolin treatment, and on account of his excellent results, he thinks it should be used in place of vaginal irrigation. In employing his method, the author attaches special value to the examination of the patient, as the cause of leucorrhœa is frequently due to constipation, chlorosis or early tuberculosis. The symptomatic treatment of the leucorrhœa is then simple and effectual. In order to investigate and treat a discharge due to local causes (gonorrhœa, tumour, inflammation, wounds, etc.) the author suggests the following procedure:

Nassauer, Münchener medizinische Wochenschrift 1912, No. 10, p. 523 and No. 11, p. 589. — Compare also Merck's Report 1909, p. 145, 1910, p. 127, and Medizinische Klinik 1912, No. 46, p. 1872.

When a bimanual examination has been made, a speculum is introduced and the vagina carefully swabbed. Then, by means of a little spoon, kaolin is spread in a thick layer over the whole surface, particularly over the cervix, and while removing the speculum, the vaginal wall is also thickly covered. The amount of kaolin applied cannot be too large. On the following day, examination usually shows that the discharge has ceased, for the entire secretion has been absorbed by the kaolin. If the discharge was copious, the kaolin will take the form of a tough, waxy mass, which can readily be removed by a swab. In these cases, as acute inflammation is present, it must be allowed to subside before the vagina may be touched with instruments; nor should treatment by means of tampons nor by irrigation be employed. Rather should the patient be given insufflations of kaolin 3 to 4 times a day by means of a suitable insufflator (so-called siccator); irrigation is only carried out if, after repeated insufflations of the powder, the discharge recommences, which generally occurs in 2 or 3 days. The mass of powder, completely saturated with the secretion, is removed by irrigation with several litres of soda solution or of chamomile infusion, and kaolin treatment is then immediately resumed. In particularly severe cases the discharge usually ceases in the course of a week, when the condition resembles that occurring after the first treatment by kaolin in less severe cases. The vagina is very dry, and the secretion which passes from the cervix and gives rise to the discharge can be observed. This secretion is not removed by swabs, nor is the cervical mucous membrane cauterized, as this promotes the appearance of secondary symptoms. Rather should kaolin be applied to the cervix, and, in the case of a gaping cervix, to the vagina as well. The powder has not only a desiccating, but also a draining action on the cervical cavity, which is thus allowed to heal. As the vagina is dry and filled with powder, the portio is not constantly in contact with pus and pus-producers and is thus protected from re-infection. Therein, according to Nassauer, rests the secret of the healing power of kaolin treatment.

The action of kaolin is due to its property of adsorption, which some authors, such as E. Friedberger and Ku-

m a g a i, consider to be bactericidal. But the chief value of kaolin is undoubtedly due to its adsorbant action, which renders innocuous those substances which maintain the discharge\*). O. Wille confirms the usefulness of kaolin treatment for leucorrhœa.

Küster and Geisse\*\*) discuss the Liermann kaolin method for disinfecting the hands. It consists in washing the hands with kaolin soap before the operation, and smearing on a paste made of kaolin, alcohol and a little azodermin. In order to compare the efficacy of the kaolin method with other methods of disinfection, the authors carried out a series of experiments with alcohol, acetone-alcohol and sublimate, which showed that the employment of kaolin-alcohol paste gave better results than that of alcohol alone, and the same results as corrosive sublimate and alcohol. The authors explain the action of kaolin paste as follows: The fine kaolin particles, which are smaller than most bacteria, are charged with alcohol and are rubbed into the finest folds and depressions of the skin, the air and sebaceous matter of the skin being displaced. Thus, by means of kaolin, the alcohol is introduced into deeper layers than is possible by ordinary washing, and its disinfecting and fixing qualities are developed where most germs exist. As the particles of kaolin remain in the deep parts of the skin after the alcohol has evaporated, the energetic disinfectant action of alcohol is renewed each time the hands are re-moistened with alcohol, for kaolin exerts a strong absorbent action on alcohol. 65 to 80 p. c. alcohol is the best to use\*\*\*).

As a remedy for wounds, kaolin, according to L. Neff, is of most use when it can penetrate into all parts of the wound. In such cases, in the author's opinion, Stumpf's hypothesis of the anti-bacterial action of the finely divided substance appears to be verified. Deep inflammatory processes, on the other hand, are not benefited by kaolin treatment, as kaolin possesses too slight an active absorbent action to affect dis-

\*) Compare Lichtwitz, Therapie der Gegenwart 1908, No. 12, p. 542.  
Wille, Medizinische Klinik 1912, No. 5, p. 193.

Küster-Geisse, Deutsche medizinische Wochenschrift 1912, No. 34,  
p. 1594.

\*\*) Compare Merck's Report 1911, p. 427.

\*\*\*) Compare the article on Alcohol, page 83 of this Report.  
Neff, Dissertation Freiburg i. B. 1912.

tant bacterial foci. Kaolin is eminently suitable as an aseptic wound dressing, as it is free from injurious secondary effects.

The internal administration of kaolin is discussed by Daxenberger, E. Bäumer and J. Schürer.

For diphtheria and scarlatinal diphtheria, Daxenberger administered a mixture of 100 grammes ( $3\frac{1}{3}$  oz) of sterile kaolin shaken up with 200 grammes ( $6\frac{2}{3}$  oz) of water or tea, a small teaspoonful of which was swallowed every 3 minutes until the fever had subsided, and then every 10 minutes until the membrane had disappeared. In every case in which this medication was used, the temperature fell in the course of a day from 39—40° C. to 36·8—37° C., and did not rise again. The membrane, the difficulty in swallowing and the glandular swelling usually disappeared with the fever; within 4 to 5 days the patients were out of bed, and at the end of a fortnight they were completely cured. Kaolin treatment can compete with serum treatment, especially if used early; it makes more work for the nursing staff, but is free from the secondary effects occasioned by serum injections. A combination of kaolin and serum treatment might lead to good results.

Bäumer obtained good results with sterile kaolin in chronic urticaria, in which external remedies have usually only a transient effect. He prescribed a tablespoonful, suspended in water, 3 times a day after meals. Its action depends upon the adsorption of certain products of metabolism in the intestine; these are thus prevented from entering the circulation, and the further development of the disease is checked.

Schürer, besides other medicaments, gave large quantities of kaolin in poisoning by fungi. On account of the difficulty of treating fungus poisoning efficaciously after the appearance of toxic symptoms, and on account of the simultaneous employment of other remedies, it is impossible to criticise the treatment. Of 6 cases described, one was fatal.

In the Annual Report of the German Hospital in Naples\*), it is shown that in this institution kaolin has been found so

Daxenberger, Medico 1912, No. 15.

Bäumer, Deutsche medizinische Presse 1912, No. 16, p. 126.

Schürer, Deutsche medizinische Wochenschrift 1912, No. 12, p. 548.

\*) Graeser, Jahresbericht des deutschen Krankenhauses Neapel 1911—1912.

invaluable in the treatment of diarrhoea and vomiting that this absolutely harmless and at the same time efficacious drug is justly resorted to again and again for the treatment of cholera, and of diarrhoea and vomiting. Kaolin, according to the Report mentioned above, should be considered a household remedy, and should be known to every mother, and should be kept in stock in the medical stores of every ship, especially if no doctor is at hand. Kaolin should be given in sufficient quantity, and when possible on an empty stomach. Adults are given 50 grammes ( $1\frac{2}{3}$  oz) several times a day — the oftener the better — until the desired result has been attained. The suspension is best prepared by pouring the kaolin on to some water in a glass, and not stirring until it has sunk to the bottom. Babies are given several teaspoonfuls of kaolin in double the quantity of water. If excretion takes place too slowly, the treatment is supplemented by enemata.

### Strophanthin.

From the substances belonging to the so-called digitalin group, A. Fraenkel chose k-strophanthin\*) for the treatment of cardiac insufficiency, because it possesses all the important characteristics of the bodies belonging to the digitalin group, while in small doses it acts rapidly and is soluble in water. The intravenous employment of the preparation, to which the author has for some time paid particular attention\*\*), is of special service in cases of acute cardiac insufficiency accompanied by pulmonary congestion in the form of oedema of the lungs. It has also proved useful in subacute insufficiency, in which it may relieve severe subjective symptoms and form a preliminary to internal digitalis therapy. Intravenous injection plays an important part in chronic cardiac insufficiency when administered in several series, especially in all cases of persistent loss of compensation, in which internal digitalis medication does not lead to the desired result. In cases of cardiac

Fraenkel, Münchener medizinische Wochenschrift 1912, No. 6 and 7.

\*) k-Strophanthin is the amorphous strophanthin obtained from Kombé seeds.

Compare Merck's Report 1911, p. 116. Fraenkel used k-Strophanthin Boehringer for his experiments.

\*\*) Compare Therapie der Gegenwart 1907, p. 56 and Archiv für experimentelle Pathologie 1907, Vol. 57, p. 79, also Merck's Report 1911, p. 117.

insufficiency in which congestion of the liver is the most prominent symptom, especially in those cases in which enlargement of the liver is accompanied by gastric disturbance and intolerance to drugs, no attempt should be made to force internal digitalis medication, but intravenous treatment should be applied at once. The serial employment of strophanthin injections is, according to the author, to be carried out somewhat as follows. If the first injection has given as good a result as is usual in cases of acute and subacute insufficiency, the repetition of the injection may be expected to bring about the renewal and deepening of the digitalis result and its permanency. But even if the typical complete action does not take place after the first injection, and only an improvement in breathing, diuresis and pulse are observed while the patient experiences a relief from the sensation of oppression, it is desirable to repeat the injections, first at short intervals and later at longer intervals. A preliminary dose of 0.5 milligramme is given, and this is repeated after 24 hours if well tolerated. As soon as the subjective or objective result of this medication has passed off, 0.75 to 1 milligramme is injected. The interval between the injections should be at least 36 hours and never less than 24 hours. At the commencement of treatment 3 to 4 injections will be required during the week, later 1 to 2 injections. With this cautious procedure no danger need be apprehended. Only the first injection is attended with danger, the patient being still under the influence of the digitalis medication which has preceded it. Threatening cumulative symptoms following repeated injections of strophanthin should, of course, not be overlooked. But, in spite of Vaquez' assertion, Fraenkel is of opinion that strophanthin is not contra-indicated in renal disease which is complicated or followed by cardiac insufficiency. In excessive renal hypertension, however, the dosage should be carefully regulated.

E. Kraus reports a case of paroxysmal essential tachycardia with continuous threatening symptoms, in which an intravenous injection of 0.001 gramme of k-strophanthin immediately brought about the desired result.

Vaquez, Bulletins et mémoires de la société médicale des Hôpitaux 1909, 1<sup>st</sup> April.

Kraus, Prager medizinische Wochenschrift 1912, p. 387.

g-strophanthin\*) was used by F. Meyer in experiments on the circulation in order to investigate the action of the preparation on the coronary circulation. The experiments were carried out on the exposed heart of a curarised dog and showed that the coronary vessels are in no way injured by g-strophanthin.

M. Schapkaiz carried out comparative experiments with regard to the action of k-strophanthin and g-strophanthin, and found that g-strophanthin approximated to the digitoxin type of action, whereas k-strophanthin possessed the definite character of strophanthin, its action being more rapid and less cumulative.

### Stypticin.

A few communications on this well known and widely used styptic were made in the course of the past year by Ph. Jung, F. Hussa, F. La Torre, W. Rübsamen and N. R. Kligermann. In climacteric haemorrhages, Jung recommends at first abrasio probatoria, which often leads to the complete disappearance of the haemorrhages, or they may return in a mild degree and finally cease altogether. But should they return, drug treatment may be tried; stypticin may then be administered, for it is very useful and sometimes very efficacious; 0.05 gramm ( $\frac{3}{4}$  grain) is given 3 times a day.

In a case of pulmonary haemorrhage, complicating scurvy in which a large amount of dark, fluid blood was brought up, Hussa employed stypticin with good effect. This symptom, which had continued for two days, promptly disappeared after 5 doses of 0.05 gramm ( $\frac{3}{4}$  grain) of stypticin.

La Torre investigated the histological changes of the uterine tissue of bitches after the administration of various constricting substances. Special reference may be made to his results regard-

\*) g-Strophanthina is crystalline strophanthin (Strophanthin Thoms) obtained from the seeds of *Strophanthus gratus*.

Compare Merck's Report 1911, p. 123.

Meyer, Medizinische Klinik 1912, No. 21, p. 869.

Schapkaiz, Dissertation Heidelberg 1912.

Jung, Deutsche medizinische Wochenschrift 1912, No. 15, p. 691.

Hussa, Wiener medizinische Wochenschrift 1912, No. 34, p. 2252.

Torre, Gynäkologische Rundschau 1912, No. 10, p. 359.

Rübsamen-Kligermann, Zeitschrift für Geburtshilfe und Gynäkologie 1912, Vol. 72, p. 272.

ing the differences in action of stypticin and ergotin. For while ergotin acts upon the muscular elements in their entirety and effects contraction or retraction in a centrifugal direction, tetanisation of the muscles and dilatation of the uterine cavity and of the lumen of the vessels, stypticin acts almost exclusively on the muscular elements of the vessels themselves and effects the contraction of the vessels and the more or less complete closure of their lumen. This different action has, according to La Torre, the same therapeutic result, i. e., haemostasis, which is brought about by a different mechanism in the two cases. Further, ergotin prevents the flow of blood to the mucous membrane by causing constriction of the vessels which pass through the inner muscular layer, while stypticin limits the flow of blood to the mucous membrane by effecting the more or less complete closure of the large vessels.

The pharmacological investigations of Rübsamen and Kligermann, which deal with the influence exerted by various drugs on the musculature of the uterus and tubes, e. g., ergotin, suprarenin, hydrastinine, stypticin, etc., show that hydrastinine, styptol and stypticin exert a markedly stimulating action on the musculature of the human tubes and uterus. This result, according to the author, shows the above named preparations to be contra-indicated in haemorrhage during pregnancy.

### Styptol.

J. König and A. Piersig have found that styptol, on account of its constricting action, is beneficial in nocturnal spermatorrhœa. Though it may not always furnish a positive result, yet it should be given a trial. J. W. Koehn confirms this to a certain extent. This author does not prescribe styptol by itself, but combines it with ergotin in the following manner: Rp. Styptol. 2.0, Ergotin. 7.0, Extr. Nuc. vomic. 3.5\*). M. Ft. capsul. No. 100. Sig.: One capsule to be taken night and morning. Robinson also recommends a combination of

König, Merck's Report 1909, p. 326.

Piersig, Zeitschrift für Urologie 1911, No. 11.

Koehn, Medical Standard 1912, August. — Allgemeine medizinische Zentral-Zeitung 1912, No. 50, p. 656.

\*) This evidently refers to the extract of nux vomica of the United States Pharmacopœia, which contains 5 p. c. of strychnine. Robinson, Journal of Urology 1912, February.

styptol and ergotin, as follows: Rp. Styptol. 1·0, Ergotin. 4·0. M. Ft. pilul. No. 30. Sig.: One pill to be taken daily.

### Sulphoform.

S. Bauer reports upon his experiences of tampon treatment with the use of sulphoform oil\*) in gynaecological practice. Acting upon the assumption that in many cases of affections of the adnexa, of metritis and parametritis, treatment by means of tampons and the rest they afford to the diseased genital organs, as well as the application of a suitable drug, by their combined action lead to a successful result, the author combined tampon treatment with the application of sulphoform oil. This was effected through a speculum with sufficiently large tampons of cotton wool, the upper third of which were soaked in sulphoform oil. The tampons were changed every second or third day during consulting hours. The application was repeated on an average 6 to 8 times, no other treatment being employed.

In 33 cases, which had resisted the absorptive treatment previously employed, the method described above brought about a cure or improvement which proved to be permanent in all cases seen after 1 to 1½ years. The patient's symptoms, which in the majority of cases consisted of pain in the back and in the abdomen and sides, were in every case relieved or reduced to a minimum. Dysmenorrhoeic symptoms were also relieved. Treatment was carried out in the interval between two periods. A large number of patients were discharged cured after the first period and only in rare cases had the treatment to be continued up to the second period. The benefit was almost always manifest after the first application of the tampons. This improvement was not confined to the local symptoms, as almost all the patients who were favourably influenced stated that their general health had also improved considerably.

Sulphoform was never observed to cause irritation or give rise to toxic symptoms. But as the sulphoform tampons, when removed from the vagina, emit a very unpleasant odour, they should be immediately thrown into a vessel filled with some fluid.

Bauer, Zentralblatt für Gynäkologie 1912, No. 20.

\*) A mixture of 1 part of sulphoform and 9 parts of olive oil.  
Compare also Merck's Reports 1910 and 1911.

**Sulphur Ointment.**

For the treatment of scabies Ehlers recommends a specially efficacious sulphur ointment which may be prepared as follows. 1 part of sublimed sulphur is carefully warmed with 2 parts of a 50 p. c. aqueous solution of caustic potash until the sulphur has dissolved; thus a yellow solution of potassium pentasulphide is produced\*). This solution, which contains  $33\frac{1}{3}$  p. c. of sulphur, is filtered, and 375 grammes of it are gradually mixed with 225 grammes of adeps lanæ anhyd. and 225 grammes of vaselin. flav. In order to bind the sulphur or sulphuretted hydrogen more efficiently, the author states that zinc hydroxide may be added; this is prepared by mixing 28 grammes of zinc sulphate with 40 grammes of caustic soda solution (20 p. c.). 5 grammes of benzaldehyde are added to give a pleasant smell, and the mixture is made up to 1000 grammes with liquid paraffin. This sulphur ointment contains 12.5 p. c. of sulphur.

Vörner prefers a different sulphur ointment (Thiolan). His prescription reads: 2 to 2.5 grammes of sulphur are dissolved in a kilogramme of fat at 50—100° C.; to this 50 to 45 grammes of oleum sulfuratum are added, and finally the freshly precipitated sulphur obtained by treating 40 to 45 grammes of calcium sulphate, and from which the water is removed as thoroughly as possible by applying absolute alcohol or pure glycerin direct to the filter. Besides this ointment, the name of which "Thiolan" as the author expressly remarks, is not a registered trade mark, Vörner recommends the application of sulphur in the following manner for the treatment of cutaneous affections. The skin is well dried and freed from fat and a solution of potassium sulphide (50 to 100 of water) is painted on; then 5 to 10 p. c. acetic acid is applied in a suitable manner (by means of an atomiser). The sulphur which separates out remains on the skin in a very finely divided condition. Sulphur applied in this way has an antihyperæmic and a desiccating action,

Ehlers, Ugeskrift for Laeger 1912, No. 32.

\*) Note. On heating sulphur with caustic potash, potassium thiosulphate is formed as well as potassium pentasulphide:  $6 \text{ KOH} + 12 \text{ S} = 2 \text{ K}_2\text{S}_5 + \text{K}_2\text{S}_2\text{O}_3 + 3 \text{ H}_2\text{O}$ . Calculated accurately, therefore, 1.14 parts of sulphur react with 2 parts of 50 p. c. caustic potash solution.

Vörner, Münchener medizinische Wochenschrift 1912, No. 35, p. 1909.

while thiolan acts rather as an antiparasitic and an emollient. The former is therefore specially suitable for seborrhœa oleosa, acne rosacea and for eczematous and follicular processes; thiolan especially for seborrhœa sicca, parasitic, fungoid and purulent affections (impetigo). In many cases it is beneficial to use the remedies alternately.

### Syrgol.

Wolffberg, like Hegner, expresses a favourable opinion on the action of syrgol in ocular affections. Bearing in mind Gros' communication regarding the increased disinfectant power of colloid silver solutions with increasing concentration, and in consideration of the fact that higher concentrations of other inorganic and organic silver preparations possess an irritative action, the author prefers syrgol, a colloidal preparation of silver\*), to the proteids of silver used hitherto. In a solution of only 1 in 1000 syrgol exercises a definite influence on suppurating conjunctivitis, but it is well tolerated by the normal eye in a concentration of 25 in 100. For the treatment of ocular affections the author recommends the use of 1 to 3 p. c. aqueous solutions, e. g., 1 p. c. solution in dacryocysto-blennorrhœa and chronic blepharo-conjunctivitis, 1 to 2 p. c. solution in simple acute follicular conjunctivitis, 2 p. c. solution in acute follicular conjunctivitis in which trachoma is suspected, 3 p. c. solution in blennorrhœa of the newborn and of adults. In the (82) cases treated by Wolffberg, the patients were given syrgol solution for treatment at home. Irritation or complications were never met with. The effect was, without exception, manifest immediately after the first instillations. Even in 1 in 500 dilution the drug proved equal in value to zinc sulphate in simple conjunctivitis.

### Tannismut.

Under this name bismuth bitannate\*) is now put on the market in the form of powder or of 0.5 gramme ( $7\frac{1}{2}$  grains) tablets. It is a light brown powder, which has a faintly acid taste and is therefore readily taken by children in tea.

Hegner, Merck's Report 1911.

Wolffberg, Wochenschrift für Therapie und Hygiene des Auges 1912, Vol. 15, p. 238.

Gros, Münchener medizinische Wochenschrift 1911, No. 50, p. 2659.

\*) Compare Merck's Report 1907, p. 52.

or other liquids. A. Soucek prescribed it for intestinal catarrh of children from 10 months to 13 years of age. Besides a suitable diet they were given 3 to 6 doses of 0·25 grammes (4 grains) of tannismut powder, or 2 to 3 tablets daily. The cases treated were selected from those in which the constitutional disturbances were not too severe (no infantile cholera), and the majority were cured after half or a whole week's treatment. In obstinate cases treatment lasted for 2 to 3 weeks. Tannismut is also efficacious in intestinal catarrh of adults, in doses of 6 to 8 tablets a day.

To patients who had for some time suffered from intestinal catarrh, E. Klindt at first gave 4 tablets a day, later 6 to 8 tablets, and finally 3 tablets. The evacuations were diminished and returned to normal after 2 to 3 weeks' treatment. The result remained permanent even if the patients kept on with their customary diet. The author never met with ill-effects after the administration of tannismut.

According to R. Polland, tannismut is especially useful in nervous diarrhoea, from which neurasthenic subjects sometimes suffer and which may follow conditions of excitement. The author also used it with benefit in enteritis and diarrhoea consequent upon mercury cures or salvarsan injections. The author states that the preparation may be taken equally well fasting or after a meal, as it never gives rise to gastric troubles. On the contrary, he observed tannismut to have a neutralising action in the stomach, for the gastric spasms and heartburn due to hyperacidity appear to be favourably influenced by the drug.

Tannismut is also of service in veterinary practice. In diarrhoea and distemper of dogs, Löwenthal administers it in doses of 1 to 2 grammes (15—30 grains). In every case it proved a satisfactory intestinal astringent and antiseptic.

### Tannoform.

According to C. Caldera and M. Gaggia, tannoform has proved a very useful drug in chronic otorrhœa. Out

Soucek, Therapie der Gegenwart 1912, No. 4, p. 189.

Klindt, Fortschritte der Medizin 1912, No. 50, p. 1581.

Polland, Fortschritte der Medizin 1912, No. 31, p. 973.

Löwenthal, Berliner tierärztliche Wochenschrift 1912, No. 52, p. 975.

Caldera-Gaggia, Archivio italiano di otologia e laringologia 1912,

Vol. 22, No. 4.

of 35 cases, which had resisted other forms of treatment, the authors obtained a complete cure in 22, a result which is probably chiefly due to the astringent properties of tannoform\*). The authors advise the following procedure. The auditory canal and meatus are first carefully cleansed and dried, a 1 to 2 p. c. alcoholic solution of tannoform is then used for painting, and this is followed by irrigation of the ear for 10 to 15 minutes. The ear is then thoroughly dried and a plug of cotton wool is inserted. When the secretion has almost completely disappeared, tannoform is insufflated in the form of powder, but not too large a quantity, as otherwise crusts are formed. This treatment is contra-indicated in acute inflammation with copious secretion, in caries of the bone, and in the presence of granulations.

#### Tests for Blood\*\*).

There are numerous publications dealing with the clinical analysis of blood, for which special interest may be claimed.

V. Ellermann and W. Dockhorn report upon the benzidine test for blood. According to Ellermann, minute amounts of blood may be demonstrated by scraping off the stain to be tested and placing a fragment of the scraped material on a piece of filter paper in a flat porcelain dish. If a little benzidine solution and then solution of hydrogen peroxide are poured on to the object to be tested, if the reaction is positive, blue lines are seen to radiate from the fragment containing blood. Dockhorn recommends for the benzidine test the benzidine and sodium perborate tablets suggested by Walter.

H. Zoepfritz recommends the following modification of the guaiacum resin test for the demonstration of blood in the stools: According to the amount of blood presumed to be present, 3 to 15 grammes of stool are mixed in a porcelain dish with about half its volume of glacial acetic acid, the mixture is poured off from the coarser constituents into a test-tube and is brought into intimate contact with 3 to 5 c. c.

\*) Compare Merck's Reports 1895—1911.

\*\*) Compare Merck's Report 1911, p. 434—437.

Ellermann, Hospitalstidende 1911, p. 1353. — Nordisches medizinisches Archiv 1912, II, No. 1, p. 44 (Lit.)

Dockhorn, Pharmazeutische Zeitung 1912, p. 165.

Walter, Merck's Report 1909, p. 140.

Zoepfritz, Münchener medizinische Wochenschrift 1912, No. 4, p. 180.

of ether, without shaking. Then the ether is poured off and is transferred to a test-tube containing some powdered guaiacum resin. This mixture is placed on filter paper which has been soaked in old turpentine oil. In the presence of blood, the paper is immediately coloured blue, or at any rate the borders of the ethereal mixture and turpentine paper turn blue. A coloration which occurs after a minute is of no significance. Inouye and Yastomi suggest another modification. They employ the acetate of the ethereal extract of the object to be tested (stool, urine, vomit), and after neutralising the free acetic acid in the ethereal extract (exudates and transudates), they first add alcohol and chloroform to increase its sensitiveness, and then a freshly prepared 5 p. c. tincture of guaiacum and ozonised turpentine oil. Wetselaar proceeds in a similar manner. Soper, however, states that it is not necessary, as is generally asserted, to use freshly prepared guaiacum tincture in order to obtain the characteristic blue coloration. He obtains equally satisfactory results by using a concentrated alcoholic solution of guaiacum resin, which he dilutes before use with alcohol in the proportion of 1:5.

B. Vas draws attention to a source of error in the phenolphthalein test, which depends upon the presence of phenolphthalein in the faeces to be tested. Therefore, before carrying out the test, the stools should be tested for phenolphthalein (taken as a medicine) by means of caustic soda solution.

According to F. Ravenna, phenolphthalein and resorcinphthalin are very useful tests for blood, and are fairly reliable for the demonstration of blood even in putrifying substrata. They may therefore serve to discover occult bleeding in the digestive organs, if the exogenous origin of the blood can be excluded. If this is not possible, F. C. van Leersum suggests the use of solution of hydrogen peroxide to wash

Inouye-Yastomi, Archiv für Verdauungskrankheiten 1912, Vol. 18, p. 223.

Wetselaar, Pharmaceutisch Weekblad 1912, No. 47. — Apotheker-Zeitung 1912, p. 962.

Soper, Journal of the American Medical Association 1911, Vol. 56, p. 263.

Vas, Deutsche medizinische Wochenschrift 1912, No. 30, p. 1412.

Ravenna, Riforma medica 1911, 18<sup>th</sup> December.

Leersum, Münchener medizinische Wochenschrift 1912, No. 6, p. 303.

the faeces and thus remove adherent blood, such as that originating from haemorrhoids. This method, of course, is not only suitable for the phenolphthalin test\*), but for all blood tests.

According to F. Michel, the leuco-malachite-green test, the guaiacum test and the benzidine test are rendered more sensitive by the simultaneous employment of pyridine. On the other hand, the alkaline reactions, such as the phenolphthalin and fluorescein tests, are not rendered more sensitive by the addition of pyridine (according to Meyer or Fleig). The author modifies Fürth's test for blood (compare Merck's Reagenzienverzeichnis) in the following manner: According to the amount of blood in the solution to be examined, 1 to 5 c. c. are added to 1 to 2 c. c. of pyridine and a few drops of caustic potash solution in a test-tube fitted with a glass stopper, and the mixture is gently boiled for a few minutes to dissolve the haemoglobin. In this way the foreign substances with an organic-catalytic action are destroyed. When cool, the liquid is mixed with an equal volume of 50 p. c. caustic potash solution and left to stand for a time. The pyridine layer which separates is transferred to a test-tube and rendered clear by the addition of a few drops of water. The mixture is again shaken up with an equal volume of 50 p. c. caustic potash solution. About 0.5 c. c. of the pyridine layer, which has separated and which is usually clear, is transferred by means of a pipette to a small porcelain crucible, 0.5 c. c. of glacial acetic acid is added and then 1 c. c. of leuco-malachite-green reagent\*\*) and finally 1 to 2 drops of hydrogen peroxide solution (1 p. c.). A green coloration denotes a positive reaction. In doubtful cases a blind test is carried out for comparison with pyridine, reagent and hydrogen peroxide solution.

\*) Compare Merck's Report 1903, p. 149.

Michel, Chemiker-Zeitung 1912, No. 11, p. 93, No. 12, p. 105.

\*\*) In place of Fürth's reagent, Michel recommends a reagent which is always freshly prepared before use. For this purpose 0.05 gramme of leuco-malachite-green base is dissolved in 10 c. c. of glacial acetic acid in a stoppered bottle, allowed to stand for a time and is then made up to 50 c. c. with water. Michel is not in favour of shaking up old reagents with chloroform, as was suggested by Fürth. The 1 p. c. hydrogen peroxide solution is prepared by diluting perhydrol with 2 to 3 p. c. acetic acid.

To test for blood in the presence of iron rust, A. de Dominicis allows a little fresh white of egg to dry on the material on a glass slide, and adds to it one drop of pyridine, one drop of a saturated, aqueous solution of hydrazine sulphate, and one drop of caustic potash solution. If the mixture is examined under the microscope, a more or less deep purple colour will be seen in the presence of blood. The micro-spectroscope will show the characteristic hæmochromogen absorption spectrum.

A new test for blood is described by M. Reich. If blood preparations or material containing blood are heated with acetone containing 10 p. c. of hydrochloric acid for several hours on a water bath under a reflux condenser, a red solution is obtained, which by itself and after the addition of ammonia shows characteristic absorption spectra. In a few weeks, presumably under the influence of the air, a beautiful green fluorescence appears and the absorption spectrum has perceptibly changed. The fluorescence is particularly striking if the fluorescent liquid is evaporated to dryness, the residue extracted with 95 p. c. alcohol and mixed with ether. A flocculent precipitate is formed and the alcohol-ether solution exhibits a beautiful fluorescence. If this solution is evaporated to dryness and the residue dissolved in isobutyl alcohol, the green fluorescence becomes most marked. The only disadvantage of this reaction as a test for blood is that the fluorescence only appears after 1 to 2 weeks.

The communications of E. Schaer and L. de Jager are of special interest with regard to the preliminaries for the examination of blood. Schaer uses chloral hydrate for the extraction of hæmoglobin. According to his instructions, the blood stain is moistened with a little acetic acid and is then macerated for 1 to 1½ hours with a 70 to 80 p. c. solution of chloral hydrate\*). The solution of blood thus obtained is tested in the usual way by means of guaiacum resin, benzidine or leuco-malachite-green reagent and hydrogen per-

Dominicis, Bollettino chimico farmaceutico 1912, Vol. 51, p. 181.  
Reich, Chemiker-Zeitung 1912, No. 15, p. 138.

Schaer, Pharmaceutical Journal 1912, Vol. 35, p. 157. Compare  
Chemiker-Zeitung 1912, No. 146, p. 1421.

Jager, Zentralblatt für innere Medizin 1912, No. 25, p. 623.

\*) Compare Merck's Report 1906, p. 135.

oxide. The author succeeded in this way in detecting the blood in a blood stain of 20 years' standing.

De Jager suggests a method in which the blood is first precipitated from the blood solutions, in order that the customary reactions can be carried out on the concentrated material. If, for example, urine is to be tested for small amounts of blood, 10 c. c. of it are added to 0.5 c. c. of concentrated hydrochloric acid and 0.25 grammes of formaldehyde. Or a mixture of 50 c. c. of hydrochloric acid (25 p. c.) and 25 c. c. of formaldehyde (40 p. c.) may be used as the reagent and 1 c. c. of this added to 10 c. c. of urine. In a short time a precipitate of formol-urea is formed, which carries down with it the blood contained in the urine (also albumin, urobilin and bile pigments). The precipitate is filtered off, washed with water until the reaction is no longer acid and when it has drained, the filter together with its contents is placed on a piece of filter paper. If the precipitate is now touched with benzidine solution and hydrogen peroxide solution, a blue stain results if blood is present. The examination of faeces is carried out in the same way, 1 p. c. hydrochloric acid being poured over the faeces and 0.3 grammes of urea and 15 drops of formaldehyde being added to the filtrate (10 c. c.).

Nippe describes a simpler method of carrying out Teichmann's haemin crystal test\*). This test, as is well known, consists in warming the blood material with sodium chloride and glacial acetic acid on a glass slide, which brings about the formation of brownish-red haemoglobin crystals, so-called haemin crystals. By the addition of glacial acetic acid, crystals of sodium chloride separate out at the same time and may interfere with the microscopic picture. The author therefore suggests the employment of a solution of sodium chloride in glacial acetic acid, or even better is the use of a solution of sodium bromide and sodium iodide, as these give rise to haemin crystals of a more intense colour. Nippe therefore recommends a solution of 0.1 grammes of potassium bromide, 0.1 grammes of potassium iodide and 0.1 grammes of potassium chloride in 100 grammes of glacial acetic acid. He prefers the potassium salts to the sodium salts because they give rise to practically no supplementary crystals. The reagent keeps well and is said to furnish very satisfactory results.

Nippe, Deutsche medizinische Wochenschrift 1912, No. 47, p. 2222.

\*) Compare Merck's Reagenzien-Verzeichnis.

H. Welsch and Lecha-Marzo suggest the employment of sodium fluoride in place of sodium chloride. They extract the blood stain with glacial acetic acid and 1-p. c. sodium fluoride solution, and evaporate the extract on a glass slide by heating, with the repeated addition of glacial acetic acid. Crystals with a red to blackish-brown colour are produced; these show a variety of forms and their chemical characteristics are like those of Teichmann's crystals.

### Thallium Acetate.

Thallium acetate,  $TiC_2H_3O_2$ , forms white crystals, soluble in water and alcohol. Years ago, as I have previously reported\*), it was recommended internally in daily doses of 0·1 to 0·2 gramme ( $1\frac{1}{2}$ —3 grains) for the treatment of syphilis and for the night sweats of phthisis, but its use had to be abandoned because it causes the hair to rapidly fall out. Nor does its antisyphilitic power appear to be as great as was at first assumed\*\*). This is shown by the recent researches of A. Buschke; he was unable to influence experimental animal syphilis by means of thallium salts. On the other hand, the author entirely confirmed the property of giving rise to alopecia possessed by thallium salts. By the use of doses of thallium acetate and thallium carbonate so minute that they could barely be estimated, he was able to bring about partial or complete alopecia in mice, rabbits, rats and monkeys. The thallium salts appear to act not peripherally but centrally, i. e., probably by way of the nervous system. The alopecia which has been observed in man after the ingestion of thallium salts would appear to be transient in nature, nor does it occur immediately, but only after some time. W. Luck and W. Marmé have shown that larger internal doses may give rise to other unpleasant secondary symptoms, such as ptalism, vomiting and diarrhoea, and thallium also appears to be a

Welsch and Lecha-Marzo, Revista de medicina y cirujia prácticas  
1912, 21<sup>st</sup> March.

\*) Compare Merck's Report 1898, p. 145.

\*\*) Compare Pozzi and Courtade, Gazette médicale de Paris 1884,  
No. 13, p. 197.

Buschke, Deutsche medizinische Wochenschrift 1911, No. 4, p. 161.

Luck, Dissertation Dorpat 1891. Marmé, Jahresbericht der gesamten Medizin 1867, I, p. 439.

cardiac poison\*). Considering the lack of reliable depilators, which are harmless and can be used for discrete areas, it seems surprising that thallium salts have not been made use of in some reliable form, or that at least attempts have not been made to apply them locally. Vignolo Lutati alone carried out superficial experiments in this direction, the results of which did not, however, prove satisfactory when repeated by Buschke. In an interesting communication, Sabouraud describes the good results obtained by external application for the removal of downy hairs round the mouth in ladies. For the treatment of hypertrichosis he suggests an ointment of the following composition: Rp. Thall. acet. 0·3, Zinc. oxid. 2·0, Vaselin. 20·0, Lanolini 5·0, Aq. rosæ 5·0. The action of this preparation, though slow, is said to be sure and lasting, without giving rise to injury or any other loss of hair. The author believes that the ointment does not destroy the downy hairs and does not get rid of them at once, but that it diminishes the length and thickness of the hairs and makes them lighter in colour. He believes that the hairs drop out and are replaced by thinner and shorter ones. If Sabouraud's statement is confirmed, thallium acetate will surely prove of value on account of the great difficulty otherwise attending depilation.

### Thigenol.

J. Trebing reports upon the employment of thigenol\*\*) in gynaecological practice. He prescribed the drug on tampons, which were placed as near as possible to the diseased area, for example behind the cervix for exudations in Douglas' pouch, and in the right or left vaginal vault for affections round the uterus. The tampons were left on an average for 24 hours and the vagina was then irrigated. Thigenol was applied in a pure form in pruritus of the vulva and anus, fissures of the anus and breasts, intertrigo, vulvitis and painful haemorrhoids. The following prescriptions have proved of special value in haemorrhoids: Rp. Thigenol 5·0, Ol. Theobrom. 20·0; fiant bacilli No. VI. Sig.: Half a bougie to be

\*) Compare Rabuteau, Gazette hebdomadaire de médecine 1874, p. 293.

Sabouraud, Revue internationale de médecine 1912, No. 18, p. 322.  
Trebing, Therapie der Gegenwart 1912, No. 10, p. 450.

\*\*) Compare Merck's Report 1902, p. 164.

introduced night and morning after evacuation of the bowels. — Rp. Thigenol 0·3, Omnopon 0·02, Extr. Belladonn. 0·01, Ol. Theobrom. 2·0; ft. suppos. Mitte tal. X. Sig.: 1 to 2 suppositories to be introduced daily. These suppositories are also suitable for the treatment of painful endometritis, affections of the adnexa and parametritis. For irrigation a 20 p. c. solution of thigenol in glycerin is used, 2 to 4 tablespoonfuls of which are added to one litre of water. Trebing is very favourably impressed with the results of thigenol treatment. Lallich also found thigenol beneficial in parametritis, etc., in the form of ointments and vaginal pessaries.

### Thiocol.

A reaction which may prove of significance for the diagnosis of hepatic insufficiency is described by D. de Sandro. It depends upon the detection of a substance in the urine after the ingestion of potassium guaiacol-sulphonate in large doses, or after its prolonged use in small doses. Its chemical composition is not yet known. It gives a characteristic green coloration with ferric chloride solution which, although not very sensitive, may be of value with a little practice. To carry out the test, a drop of ferric chloride solution is placed in a test-tube and the urine to be tested is poured on to it, care being taken not to produce a precipitate of phosphates. The best way is to add the urine gradually in small amounts. To guard against error in the presence of bile pigments, acid is added to the green mixture. If bile pigments are present, the green colour persists, but if it is caused by the unknown substance, the colour disappears. The green coloration occurs in healthy and diseased subjects after the ingestion of thiocol, but in the presence of hepatic insufficiency it becomes inconstant and indistinct according to the degree of insufficiency. In advanced cirrhosis the reaction no longer occurs.

### Thiocyanates.

Since F. Franz has experimentally proved that the neutral thiocyanates are non-toxic, these might be more generally used

Lallich, Schweizer Korrespondenzblatt 1912, p. 616.

Sandro, Riforma medica 1912, Vol. 28, p. 113.

Franz, Merck's Report 1911, p. 439. — Arbeiten aus dem kaiserlichen Gesundheitsamt, Vol. 38, No. 4.

in therapeutics\*). Zoltán v. Dalmady has recently again drawn attention\*\*) to the usefulness of sodium thiocyanate. He has for many years used the preparation, according to the following prescription, for the lightning pains of tabes, for arterio-sclerosis and for angiospastic migraine:

Rp. Sod. thiocyan.	1·5—2·5 grammes (24—40 grains)
Aq. destill.	140·0—180·0 grammes ( $4\frac{2}{3}$ —6 oz)
Syrup.	10·0—20·0 grammes ( $1\frac{1}{2}$ — $2\frac{1}{3}$ oz)

M. Sig.: 3 to 5 tablespoonfuls to be taken daily.

The author prescribes 0·15 to 0·25 gramme ( $2\frac{1}{3}$ —4 grains) as a single dose, and 0·45 to 1·25 gramme (7—20 grains) as a daily dose. Unpleasant secondary effects were never observed. Von Dalmady only once met with thiocyanate coryza, in a case in which the drug had been experimentally used in bronchial asthma.

In tabes the analgesic action of sodium thiocyanate sets in on the third to fifth day of the medication, which appears to exclude the possibility of its acting by suggestion. Occasionally it effects the complete cessation of the attacks of pain, but more commonly the pain is merely alleviated and the attacks occur with less frequency. The effect seems to last for some time, for the author observed that the action continued after using it for some weeks, and even after the medication had been discontinued for 2 to 3 weeks. Habituation to the drug was not easily established. Sodium thiocyanate appears in time to cause slight lowering of the blood pressure.

Sodium thiocyanate is particularly valuable in angiospastic migraine and is also of good service in sympathetic neuroses.

A new thiocyanate preparation is recommended by J. Nerkling, A. Lohmann, G. Diena, A. Scheuer, Wagner,

\*) Compare Merck's Reports 1909—1911.

Dalmady, Wiener klinische Wochenschrift 1912, No. 21.

\*\*) Compare Merck's Report 1909, p. 316.

Nerkling, Medizinische Klinik 1912, No. 6. — Allgemeine medizinische Zentralzeitung 1912, No. 15.

Lohmann, Archiv für Zahnheilkunde 1911, No. 8. — Zahnärztliche Rundschau 1913, No. 3.

Diena, Biochemische Zeitschrift 1912, No. 1 and 2.

Scheuer, Prager medizinische Wochenschrift 1912, No. 2.

Wagner, Zahnärztliche Rundschau 1913, No. 4.

G. Steinkamm, G. Luda, E. Neumann, Schubert and Meyer. These authors state that it is indicated in arteriosclerosis, tabes, anaemia, uric acid diathesis, angina, hay fever, and in a variety of dental diseases, such as caries and stomatitis. This is "Rhodalzid", a thiocyanate-albumin preparation, containing a definite amount of thiocyanate, which is put on the market in the form of tablets. One tablet is given 3 times a day after meals, after a week 2 tablets a day are administered, the medication is then discontinued for a week and finally one tablet a day is given for a fortnight. The preparation is said not to give rise to harmful secondary effects. Brehmer, who carried out experiments on himself, doubts this, for after the ingestion of 3 tablets he was troubled with gastric disturbance, rigors, vomiting and foul breath. The author also refuses to accept the hypothesis advanced by Michel that the presence of thiocyanates in the saliva prevents the occurrence of caries, as he has met with caries when the saliva contained a large amount of thiocyanate. Lewinski has met with equally unpleasant experiences in some of his patients.

### Thymol and Thymol Derivatives.

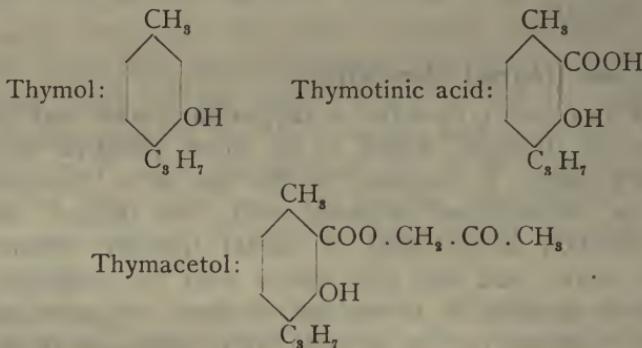
Lenher and Crawford suggested a new test for the detection of titanium, which is far more sensitive than the customary tests. It consists in the use of a solution of thymol in concentrated sulphuric acid. As thymol forms a yellow solution in this acid, it should first be dissolved in alcoholic acetic acid and this mixed with the sulphuric acid in order to produce a colourless solution. In preparing the reagent it should not be diluted with water, as it is thus rendered less sensitive. For the same reason the sulphuric acid used should not have a lower specific gravity than 1.725. The authors state that the reagent will keep for a long time if it is kept protected from light.

Steinkamm, Zahnärztliche Rundschau 1912 and 1913, No. 4.  
Luda, Moderne Medizin 1912, No. 7.  
Neumann, Ash's Wiener Vierteljahres-Fachblatt 1912, August.  
Schubert, Therapie der Gegenwart 1912, No. 7.  
Meyer, Deutsche zahnärztliche Wochenschrift 1912, July.  
Brehmer, Zahnärztliche Rundschau 1913, No. 2.  
Lewinski, Zahnärztliche Rundschau 1913, No. 3.  
Lenher-Crawford, Chemiker-Zeitung 1912, p. 1072.

The test is performed by adding the reagent to the solution of titanium, when a beautiful red colour is produced in proportion to the amount of titanium present. It is said that as little as 0.006 to 0.0001 grammes of  $TiO_2$  can readily be detected in this way. The red colour disappears on heating the mixture, but returns as it cools. The test is influenced by the presence of tungsten, but not by the presence of hydrochloric acid or phosphoric acid.

C. Bachem describes two derivatives of thymol, which appear to be suitable for therapeutic employment, viz., thymotinic acid and thymacetol.

Thymotinic acid forms white crystals, soluble in alcohol, ether, benzol, chloroform, and slightly soluble in hot water. It gives a bluish-violet coloration with ferric chloride, which may serve as a test for the presence of the acid in the urine. According to the author's experiments, thymotinic acid is apparently only slightly toxic for animals, although it is comparatively rapidly absorbed. The constitution of the acid:



suggests a similar action to that of salicylic acid, but experiments in proof of this are lacking. The same applies to thymacetol (thymotinic acid acetone ester), the constitution of which is analogous to that of salacetol\*). It is a white, crystalline powder, melting at  $75^\circ C.$ , insoluble in organic solvents and in fatty oils. According to Bachem, pharmacological investigation has shown that thymacetol, like thymotinic acid, is comparatively slightly toxic for the animal organism, as rabbits readily tolerate 2 to 3 grammes. It is readily absorbed,

— Bachem, Berliner klinische Wochenschrift 1912, No. 44, p. 2086.

\*) Compare Merck's Report 1893, p. 78.

both on internal and external application. If the 2 p. c. ethereal solution of the preparation is applied to the skin of a rabbit in a suitable manner, the thymotinic acid reaction can be obtained in the urine by means of ferric chloride on the following day. Thymacetol possesses no evident antiseptic action, but it has a marked effect as a local anaesthetic. A few milligrammes applied to a rabbit's cornea bring about complete loss of sensation in 2 to 3 minutes, which persists for about 30 minutes. Thymotinic acid, although it also has an anaesthetising effect, at the same time acts as a corrosive. This suggests that the anaesthesia produced by thymacetol and the absence of corrosive action are chiefly due to the acetone substitutes. The solutions in organic solvents are said to be little suitable for practical purposes. Bachem recommends a solution of thymacetol in ethoxy-propionic acid menthol ester (1:10). The author expects thymacetol to furnish good results in cases in which the nerve endings are exposed (burns, gastric and laryngeal ulcers), and the solution mentioned above to prove useful in irritative catarrhal conditions of the pharynx and larynx.

#### Tincture of Pulsatilla.

Preparations of pulsatilla were formerly applied both internally and externally in various ocular affections, toothache, rheumatic pains, chronic eczema, nervous troubles, neuralgia, acute epididymitis, and in catarrhal affections of the respiratory passages; at present, however, they are but little used. A communication by Wilcke is therefore of interest; he obtained striking results by the use of tincture of pulsatilla in pertussis and bronchitis. As tincture of pulsatilla has always been stated to possess a sedative action, it would be justifiable to repeat Wilcke's experiments. The author gave to adults 10 to 20 drops several times a day, and to children 5 to 10 drops, and never met with harmful secondary effects. The danger of poisoning from tincture of pulsatilla would certainly be less than from opiates.

The action of tincture of pulsatilla is most probably chiefly due to the pulsatilla camphor, so-called anemonin, which is preferable to tincture of pulsatilla on account of accuracy of dosage. It forms yellowish-white crystals, melting at 152° C.,

of the chemical formula  $C_{10}H_8O_4$ , and which are soluble in alcohol. As an antispasmodic and anodyne it has, according to Bovet, proved of value in pertussis, bronchitis, asthma and dysmenorrhœa. For adults it is prescribed twice a day in doses of 0.025 to 0.05 grammes ( $\frac{2}{5}$ — $\frac{3}{4}$  grain); 0.1 grammes ( $1\frac{1}{2}$  grains) for a dose and 0.2 grammes (3 grains) during the day are considered the maximum doses.

### Tiodine.

In connection with the investigations of Patschke, reference may be made to Travaglino's communications; he carried out a number of clinical experiments with tiiodine (thiosinamin-ethyl-iodide) on arterio-sclerotic subjects. In opposition to Patschke, the author did not observe tiiodine injections to exert an influence on the patient's subjective symptoms, and he frequently met with painful local symptoms of irritation at the site of injection. But the blood pressure was always lowered after 3 to 6 injections, and it was reduced to a greater extent the higher it had previously been. Between the injections the blood pressure rises somewhat, but during the course of tiiodine treatment it never rises so high as it was before treatment. It usually remains at the same level for some months after the treatment\*).

### Titanic Acid.

K. A. Hofmann found that so-called chromotropic acid (1,8-dioxynaphthalene-3,6-disulphonic acid\*\*) was a sensitive test for tetravalent titanium. A minute amount of titanic acid (titanium dioxide), dissolved in hydrochloric or sulphuric acid, gives an intense red coloration with chromotropic acid. O. Hauser and A. Lewite have demonstrated that all phenols react in a similar way with titanic acid, so that titanium dioxide may be used as a test for phenols, and as a test for

Bovet, Merck's Bericht 1889, p. 12. Compare also Merck's Index 1910, p. 38.

Patschke, Deutsche medizinische Wochenschrift 1911, No. 33, p. 1513.  
— Merck's Report 1911, p. 440.

Travaglino, Nederlandsch Tijdschrift voor Geneeskunde 1912, No. 20.

\*) Compare Merck's Reports 1907 and 1911.

\*\*) Compare Merck's Report 1911, p. 222.

Hauser-Lewite, Berichte der deutschen chemischen Gesellschaft Berlin 1912, Vol. 45, p. 2480.

the oxy-group in general. According to the authors, a concentrated solution of titanic acid in hydrochloric or sulphuric acid gives a blood-red coloration with phenol, cresols, thymol, guaiacol, hydroquinone, pyrocatechin, resorcin, orcin, vanillin, phloroglucin, pyrogallol, naphthols and certain oxynaphthalene-disulphonic acids. Dilute titanic acid solutions give a yellowish-red to deep red coloration with pyrocatechin and pyrogallol, and the dioxy-naphthalene-disulphonic acids a violet to red coloration, according to the concentration of the sulphuric acid used. To carry out the test, a few drops of concentrated titanic acid solution in cold fuming hydrochloric acid, or strong sulphuric acid, are added to a few decigrammes of phenol and heated, if necessary, after the addition of a few drops of alcohol or acetone as a solvent. The mixture assumes a deep red to violet colour. The coloration is less intense when monoxycarbonic acids are used. Salicylic acid, for example, gives a reddish-yellow colour.

### Tropacocaine.

In connection with my former communications on tropacocaine, attention may be drawn to a paper by A. W. Gregori, in which the author describes the value of tropacocaine hydrochloride in spinal anaesthesia, based on a larger number of cases. The author's favourable opinion confirms the statements which have already been made by a large number of observers\*). Gregori attaches special importance to the correct position of the patients after the application of the drug. He adopted a horizontal position with the head slightly raised; he also found that the rare complications of tropacocaine anaesthesia could be still further reduced by using more dilute solutions of tropacocaine. He usually employed a freshly prepared 0.5 p. c. solution in doses of 5 to 10 c. c.

According to Goldberg, who reports upon 300 cases of spinal analgesia by tropacocaine, the disturbing consequences of the anaesthesia, such as collapse, etc., are commoner in women than in men. He observed them in 9 p. c. of his cases. He injected a 3 p. c. aqueous solution of tropacocaine hydro-

Gregori, Schmidt's Jahrbücher der in- und ausländischen gesamten Medizin 1912, Vol. 316, No. 3. — Archiv für Chirurgie 1912, Vol. 28, p. 316.

\*) Compare Merck's Reports 1892—1911.

Goldberg, Zentralblatt für Chirurgie 1912, No. 19, p. 648.

chloride in doses of 0·03 to 0·1 gramm of tropacocaine at the level of the third or fourth lumbar vertebra, and then kept the patients in a sitting posture for 3 to 5 minutes. 88 p. c. of the cases were completely successful, 6 p. c. were partially successful and in 6 p. c. the result was negative. An intimate knowledge of the method is required, for the author states that with increasing experience the failures became more and more rare.

These experiences are in agreement with Schütte's views; he attributes the unsatisfactory results of spinal analgesia which have been recorded to lack of knowledge of this method of inducing anaesthesia with consequent faulty technique. He is greatly in favour of spinal analgesia, and with regard to technique he lays special stress upon median puncture into the dural sac. Jaschke considers the most suitable preparation for spinal anaesthesia to be tropacocaine in conjunction with scopolamine-morphine dawning sleep. As regards the effect of the anaesthetic, the author states that the method only fails in isolated individuals, and in these subcutaneous injection is no more successful. According to Jaschke, every trace of disinfectant should be removed from the skin by washing with saline solution before the lumbar application; this guards against subsequent headaches.

G. Acconci and N. M. Multanowski also express themselves well satisfied as to the value of tropacocaine anaesthesia. Acconci administered over 200 lumbar injections of tropacocaine in his gynaecological practice, more especially in lengthy operations in elderly and debilitated women, and obtained good results in every case. Multanowski describes 150 cases in which tropacocaine was employed in patients between the ages of 16 and 86. Complete anaesthesia was obtained in 132 cases, sufficient anaesthesia in 6 cases; in 7 cases supplementary general anaesthesia was required, and only in 2 cases did it fail entirely. In 3 cases anaesthesia failed because it was found impossible to reach the spinal canal. But even in the cases in which chloroform anaesthesia had to be used, the action of tropacocaine was evident in that only very small amounts of chloroform were required to bring

Schütte-Jaschke, *Zentralblatt für Gynäkologie* 1912, No. 41, p. 1355.

Acconci, *Deutsche medizinische Wochenschrift* 1912, p. 1816.

Multanowski, *Wratschebnaja Gaceta* 1912, No. 27.

about full anaesthesia. The secondary effects of spinal anaesthesia (the patients were principally neurasthenics) were never serious and never jeopardised the patient's life; no case of collapse nor of paralysis of the respiratory centre nor of serious paralysis of the lower extremities was encountered. Nausea, vomiting, involuntary defaecation only occurred in a few cases, and headaches were met with especially in alcoholic subjects. Transient rise of temperature was also observed. As a result of his experience, the author has come to the following conclusions: Spinal analgesia, thanks to the perfected technique introduced during the last few years, is no longer so dangerous as during the first years following its introduction and should therefore be more widely used. — The only contra-indications are septic and pyæmic processes, in which the trauma of the vertebral column (caused by the injection) may give rise to an area of diminished resistance for the micro-organisms. — Spinal analgesia is of special value to the country practitioner; it may enable him, in case of need, to perform an operation without special assistance.

P. Guillermín has investigated the pharmacological action of tropacocaine. His results agree with those of other observers, inasmuch as he also considers the preparation to be a useful local and spinal anaesthetic and which is comparatively slightly toxic.

### Tryen.

Tryen is, according to Abel, para-iodo-orthosulpho-oxy-cyclo-hexatrienopyridine, a yellow powder, without odour, soluble in hot water and harmless to the human organism when given in suitable doses. As it appears unchanged in the urine shortly after ingestion, the author assumes that it does not become fixed in the organism, so that it does not give rise to iodism. In only 6 p.c. solution tryen possesses marked bactericidal properties and these are considerably increased in stronger concentrations (10 to 20 p.c.). Abel never met with troublesome secondary effects; at most the patients complained of a transient slightly burning sensation after the application of the drug.

Guillermín, Revue trimestrielle suisse d'odontologie 1912, No. 2.  
Abel, Medizinische Klinik 1912, No. 50 and Berliner klinische  
Wochenschrift 1912, No. 53.

For the treatment of vaginal catarrh, Abel uses 10 to 20 p. c. tryen gauze, which he introduces into the vagina in such a way that it more or less envelopes the cervix and fills up the vagina. The patient draws it out after 24 hours and the application is repeated two or three times, according to the severity of the case, at weekly intervals. The vagina is not irrigated during this treatment. Simple vaginal catarrh is said to be so greatly improved after 3 to 4 applications of tryen gauze that the discharge disappears permanently. Its application has also proved useful in obstinate gonorrhoeal affections, but in these 20 p. c. tryen gauze should always be used. To guard against infection of the vagina from the urethra, the latter is treated with small pencils of tryen, prepared with cocoa butter. Possibly the morbid process may be favourably influenced by internal medication with tryen. The author has not conducted experiments on these lines, but believes that 0.5 gramme ( $7\frac{1}{2}$  grains) may be administered 3 times a day. Tryen is serviceable in gonorrhoea of children; it is introduced into the vagina in the form of small pessaries.

If the discharge is due to disease of the cervix, plugging with tryen is not sufficient, but the gauze must be introduced into the cervix with the help of a speculum. If the endometrium is diseased, the uterus must be packed with sterile tryen gauze. In inflammatory affections of the adnexa, tryen plugs are also beneficial, though they cannot bring about a cure. In the form of powder tryen may be used to sprinkle on wounds.

### Tryparosan.

Tryparosan is, according to S. W. Lewaschew, a substance first prepared by Benda by the introduction of chlorine into the para-fuchsine molecule. According to the investigations of Roehl in the Ehrlich Institute in Frankfort, it has proved to be less toxic than para-fuchsine, at the same time it acts more powerfully on microbes. Lewaschew received tryparosan from Ehrlich in order to compare its therapeutic efficacy with that of para-fuchsine in typhus. But he decided to try the drug in tuberculosis and chose for this purpose the most advanced cases in his clinic, patients in the last stage of the disease,

with cavities and with a large numbers of tubercle bacilli in the sputum. In order to avoid gastric irritation, pains and vomiting, he administered the preparation finely ground and mixed with milk sugar, talc, powdered marshmallow root, etc., in soluble capsules or cachets. He usually administered it according to the sex, age, general state of health or condition of the digestive organs of individual patients 4 to 8 times a day in doses of 0·5 to 1 gramm (7½—15 grains), a quarter to half an hour after meals. In every case a small amount was prescribed at first (1 to 2 grammes [15—30 grains] a day) to determine the patient's tolerance, then the daily dose was rapidly increased to 3 to 8 grammes (45—120 grains). According to the intensity of the morbid symptoms, the medication had to be continued for weeks or months, but as soon as the desired effect had been obtained, the dose was correspondingly reduced. The only secondary effects observed were loss of appetite and red spots on the skin, which disappeared on discontinuing the drug and which did not trouble the patient.

The action of tryparosan was manifested by a reduction in the febrile temperature; this the author considers to be not symptomatic but rather in the nature of a specific action on the tubercle bacilli, similar to that of quinine on the plasmodia of malaria. Tryparosan also in time facilitates expectoration and reduces the amount of sputum, while it improves the condition of the lungs.

### Trypsin.

M. Saidmann has made use of trypsin therapy\*) in local suppurative tuberculosis and has obtained noteworthy results. The technique of trypsin administration, according to the author, is as follows: It is best to use a freshly prepared, 1 p. c. solution of trypsin in sterile normal saline solution; the site of injection is disinfected with tincture of iodine and 1 to 2 c. c. of the trypsin solution are injected into the neighbourhood of the tuberculous area, or better still, into the tuberculous focus itself. After the injection a dressing or a piece of adhesive plaster is applied. If several injections are required, they are repeated once a week. The secondary effects of the injections are insignificant. As regards the action

Saidmann, Wiener klinische Wochenschrift 1912, No. 5, p. 204.

\*) Compare Merck's Report 1911, p. 446.

of trypsin, according to Saidmann, it is partly of the nature of a chemotactic action of the ferment on the leucocytes and partly a purely chemical action of trypsin, i. e., it effects the digestion of the pus. The author concludes that the therapeutic effect of trypsin is greater than that of iodoform-glycerin, which only possesses a chemotactic action on the leucocytes. The results of the trypsin treatment of tuberculous glandular abscesses were so good that the author also tried the injections for tuberculous fistulas. In two cases he effected the cure of the fistulas; in a third case the fistula closed, but broke open again and did not close with further treatment. The treatment proved successful in spina ventosa, but it failed in a case of hygroma of the tendon sheath, and in a case of ganglion of the superficial flexor tendons of the hand, probably because the author left off treatment too soon.

A. Sticker and S. Rubaschow have contributed to our knowledge of carbenzyme treatment. As a result of their experimental and clinical investigations they came to the conclusion that the preparation is sterile and that its therapeutic efficacy is less affected by treatment with chloroform, alcohol and potassium permanganate than is that of trypsin. This agrees with the results obtained by M. Winckel, who found that the trypsin bound to carbon in carbenzyme resists the action of the gastric juice. Sticker and Rubaschow found further that carbenzyme suspended in glycerin is as efficacious as in soda solution, that it does not attack normal tissue, but rather digests broken down dead tissue and cystic contents. It only gives rise to a severe reaction after injection in the presence of acutely inflamed tissue or of areas under great tension. The drug renders tuberculous pus liquid, serous and blackish and endows it with the property of digesting albumin, which lasts as long as 10 days. Its therapeutic effect is specially evident in breaking down tuberculosis of the soft parts, in cold abscesses, hygromata and softened lymphatic glands. In ganglia the contents are digested, while the connective tissue sac remains unchanged\*).

Sticker-Rabuschow, Berliner klinische Wochenschrift 1912, No. 44,  
p. 2074.

Winckel, Münchener medizinische Wochenschrift 1912, No. 50,  
p. 2734.

\*) Compare Merck's Reports 1910, p. 136.

### Tungsten, Colloid

In place of bismuth salts, R. Krüger recommends colloid tungsten for the production of a shadow in the X ray examination of the gastro-intestinal tract; it is put on the market in the form of a black powder without odour or taste. According to v. Hayek, the preparation is wholly non-toxic, and this was confirmed by Krüger in his experiments on rabbits. By means of an oesophageal tube he gave these animals 5 to 25 grammes. They showed no signs of disease, took their food well and behaved exactly as before. Thereupon the author tried the preparation for human beings, giving 25 to 80 grammes. He did not observe toxic symptoms in a single case, none of the patients showed disturbance of the gastric or intestinal functions, stomatitis or nephritis. Comparisons between bismuth and tungsten radiographs taken in the same individual showed no difference; the outlines of the stomach were equally defined in the two cases.

### Uranium Acetate.

Uranyl acetate in 2 p. c. solution was suggested by Kowalewsky nearly 30 years ago as a test for albumin, but was not generally adopted on account of its supposed uncertain significance and insufficient sensitiveness\*). A. Oszacki's work shows, however, that the reagent gives a sufficiently definite reaction, as it does not precipitate other nitrogenous substances occurring in the body fluids, and, on the other hand, it appears to be highly sensitive, for the author finds it suitable for the quantitative precipitation of albuminous substances. These properties caused the author to employ uranyl acetate to render serum free from albumin; this permits the estimation of the remaining nitrogen in the blood or serous fluids, which is sometimes required by the clinician. For this purpose a reagent is required which completely precipitates albuminous

Krüger-Hayek, Münchener medizinische Wochenschrift 1912, No. 35, p. 1910.

Kowalewsky, Merck's Reagenzien-Verzeichnis 1908, p. 141.

Oszacki, Zentralblatt für innere Medizin 1912, No. 47, p. 1165.

\*) Uranyl acetate is unsuitable for the detection of albumin in the urine, because the urine always contains phosphates. The reaction would have to be performed in a solution acidified with hydrochloric or nitric acid, to avoid errors due to uranyl phosphate.

substances, which does not carry down other nitrogenous substances and does not split off nitrogenous complexes. The author finds that uranyl acetate satisfies all these requirements. The estimation of the remaining nitrogen is simple. The serum to be tested is diluted with water, 1·5 p. c. aqueous solution of uranyl acetate is added, it is filtered, sufficiently evaporated in a suitable glass flask (for Kjeldahl estimation) and the nitrogen is estimated according to Kjeldahl's method (in the presence of an excess of uranyl acetate). For this investigation at least 15 c. c. of serum are required, and it is best, if possible, to use 50 c. c.

### Urea.

G. Picot draws attention to the diuretic action of urea. By prescribing urea in various cases of oliguria he obtained a favourable effect on diuresis, and in one case of uræmia it even saved life, although the patient came under treatment in a moribund condition. The increased renal secretion was always accompanied by an improvement in the general health. As it has been assumed hitherto that uræmia is caused by urea which has not been excreted but has remained in the blood, and by its products of decomposition, the author, on account of his successful administration of urea, has come to the conclusion that uræmia is caused by other substances, e. g., by nitrogenous bodies. In one patient it was shown that the percentage of urea in the blood was not diminished after the medication; in spite of this the amount of urine was increased and the general condition improved. The author assumes a sort of antagonism between the substances giving rise to oliguria, somnolence and dyspnoea on the one hand, and urea on the other hand, which would account for the promotion of diuresis by the ingestion of urea.

I have previously reported upon the dosage of urea\*). One tablespoonful of a 5 p. c. aqueous solution is given hourly at first, and in the course of some days a 7·5 p. c. and then a 10 p. c. solution is used. 10 to 20 grammes ( $\frac{1}{3}$ — $\frac{2}{3}$  oz) may be given daily.

Picot, Journal d'urologie médicale et chirurgicale 1912, Vol. 2,  
No. 2.

\*) Merck's Report 1896, p. 163.

### Ureabromine.

H. Böhmig and E. Jach carried out therapeutic tests with ureabromine\*), which was introduced into therapeutics by Fischer and Hoppe. Böhmig prescribed it for epileptics who were suffering from acne, loss of appetite and cardiac debility consequent upon lengthy courses of treatment by bromides, or for those who were anaemic and badly nourished; after two to three weeks' treatment the cutaneous affections disappeared, and the cardiac action had improved; in certain cases the appetite improved and there was a gain in weight. The author attaches special importance to an observation in a case of epilepsy, in which the symptoms of bromism had disappeared under ureabromine treatment, and when the administration of bromine was repeated, the symptoms did not reappear as rapidly as the first time. Ureabromine also proved beneficial in two severe cases of chorea in older children, both complicated by cardiac lesions. In a surprisingly short time ureabromine brought about repose, so that better sleep and better nutrition became possible. It is also useful in nervous conditions of anxiety and insomnia. Jach obtained equally favourable results. With regard to the chemical examination of ureabromine, reference may be made to the communications of A. Biltz.

### Urethane.

Urethane, often called ethyl carbamate and also ethylurethane, which has been much used in the treatment of insomnia, eclampsia, tetanus and various conditions of excitement, is carbaminic acid ethyl ester,  $\text{CO}(\text{NH}_2)\text{OC}_2\text{H}_5$ . It forms white crystals, which dissolve readily in water and alcohol; melting point 48—50° C.

According to F. Bertling, this preparation has proved most useful as a hypnotic and an antispasmodic for children. It is a good soporific for children who are restless in consequence of nervous excitement, of hunger due to therapeutic

Böhmig, Psychiatrisch-neurologische Wochenschrift 1912, No. 47.  
Jach, Therapie der Gegenwart 1912, No. 10.

\*) Compare Merck's Report 1911.

Fischer-Hoppe, Berliner klinische Wochenschrift 1911, No. 41.

Biltz, Pharmazeutische Zentralhalle 1912, No. 10.

Bertling, Berliner klinische Wochenschrift 1912, No. 4, p. 147.

reasons or of pains from wounds, stomatitis and other inflammatory affections. The drug is valuable in the nocturnal restlessness of babies during the first 3 months of life, whether this be due to nutrition or to cerebral affections. The following doses are given, but may be exceeded without apprehension and may be repeated as frequently as desired: At the age of 1 to 5 months 0·5 to 0·9 grammes ( $7\frac{1}{2}$ —13 grains); 6 to 12 months, 1 grammme (15 grains); 1 to 2 years, 1·5 grammes (24 grains); and at 2 years and over, 2 grammes (30 grains).

Urethane is a safe antispasmodic in toxic convulsions, and is therefore preferable to chloral hydrate. For convulsions 1·5 to 2 grammes (24—30 grains) are given by mouth, or 2 to 3 grammes (30—45 grains) rectally.

Urethane is also useful in prolonged nervous cases of pertussis; several doses should be given during the evening and these should not be too small. It should also be tried in spasmophilia, both in the latent and in the manifest stages, in flatulent bronchitis in place of chloral hydrate, in cardiac lesions and in the delirium so frequent after pneumonia in children. The following prescriptions may be recommended:

Rp. Sol. Urethani            2·0: 40·0 grammes (30 grains in  $1\frac{1}{3}$  oz)  
 Liquor ammon. anis.    0·5 grammme (10 min.)  
 Mucil. acaciae            1·0        „        (17 min.)  
 1 tablespoonful = 0·8 grammme (12 grains).

Rp. Sol. Urethani            2·0: 10·0 grammes (30 grains in  $1\frac{1}{3}$  oz)  
 Syrup. cinnamom. ad 20·0        „        ( $\frac{2}{3}$  oz)  
 1 tablespoonful = 1·3 grammme (20 grains).

Rp. Urethan.                3·0 grammes (45 grains)  
 Syrup.                ad 30·0        „        (1 oz)

Rp. Sol. Urethani            2·0: 10·0 grammes (30 grains in  $1\frac{1}{3}$  oz)  
 Aq. menth. pip.        5·0        „        (90 min.)  
 Saccharini q. s.  
 1 tablespoonful = 2 grammes (30 grains).

Rp. Sol. Urethani            5·0: 50·0 grammes (75 grains in  $1\frac{2}{3}$  oz)  
 Acac. gummi                1·0 grammme (15 grains)  
 Liquor ammon. anis.    0·5        „        (10 min.)  
 Saccharini q. s.  
 1 spoonful = 1 grammme (15 grains).

**Uric Acid.**

According to Falkenstein, uric acid, given subcutaneously, is a suitable means of increasing phagocytosis, which in its turn prevents the deposition of uric acid in gouty joints and so brings about the cure of gout. For his therapeutic experiments he used a 1 p. c. aqueous suspension of finely powdered uric acid, to each 2 c. c. of which 0.0075 grammes of cocaine hydrochloride and 0.00005 grammes of adrenalin were added\*). The injection of this mixture is painless and remains so for 5 to 7 hours. The site of injection becomes white, while the surrounding area reddens and becomes slightly swollen. After 5 to 7 hours severe itching usually commences and increases until the part becomes tolerably painful, at the same time the pain due to gout ceases. Only in isolated cases and in very sensitive persons is the local reaction, which apparently assists the therapeutic action of uric acid, more severe and lasting. But it always disappears and never leads to abscess formation. The injection is made above the diseased joint. If two injections are to be given, the sites chosen must be far enough apart to guard against the consequent inflammatory areas becoming contiguous. In delicate women not more than two injections are given at first, otherwise the number of injections and their repetition are regulated according to the nature of the case. If, for instance, the pain should pass to another joint, an injection may be given above it after 5 hours, and so on as often as may be necessary, for the action of the injection is almost entirely restricted to the joint beneath. In severe cases the injections may be repeated on several consecutive days. When the pain has yielded, an interval of 8 to 10 days is allowed, until the local symptoms due to the injection have passed away. Then two consecutive injections are given above joints which have been affected previously, an interval similar to the above being allowed between each couple of injections, until at least 12 injections have been given. In chronic gout, series of injections will be allowed to alternate with intervals of one or more months.

Falkenstein, Medizinische Klinik 1911, No. 45, p. 1724.

\*) This solution is issued in sterile ampoules ready for use under the name of "Urosemin".

On the strength of Falkenstein's statements, P. Wolfer gave injections of uric acid in several cases of gout, in order to observe the effect upon uric acid excretion, upon which it certainly should exert an influence. In so far as a conclusion can be drawn from the few cases observed, the injections apparently do lead to an increased excretion of uric acid, but otherwise the author observed no evident benefit from this treatment.

### Uzara.

The employment of this drug and of its preparations is reported upon by Sell, Wieland, Waldow and Gühne, O. Hirz, A. Eisenheimer, E. Müller, F. Engels, J. Schaffmann, L. Roth, Schreyer and Rieck\*). Uzara is put on the market in the following forms:

Uzara tablets, of which adults are given 3 to 4, children 1 or more, every 2 hours.

Liquor Uzara, of which adults are given from 1 gramm (17 min.) to 30 drops, and children 6 drops or more, every two hours.

Uzara suppositories, for children and adults.

According to the authors mentioned above, uzara, given internally or rectally, is a good remedy for diarrhoea. It has proved highly beneficial in diarrhoea due to various causes, e. g., in acute diarrhoea of children, dysentery, diarrhoea of typhoid, ptomaine poisoning, amœbic dysentery; and good results may be expected from it in colicky enteralgia and in dysmenorrhœa. Rieck obtained very satisfactory results by its use in a case of Graves's disease in a woman.

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Wolfer, Medizinische Klinik 1912, No. 39, p. 1581.

Sell, Beiträge zur Klinik der Tuberkulose 1912, Supplement III, p. 71.

Wieland, Schlesische Ärztekorrespondenz 1912, No. 13.

Waldow-Gühne, Archiv für Schiffs- und Tropen-Hygiene 1912, No. 6.

Hirz, Münchener medizinische Wochenschrift 1912, No. 40.

Eisenheimer, Deutsche medizinische Wochenschrift 1912, No. 51.

Müller-Engels-Schaffmann-Roth-Schreyer-Rieck, Allgemeine medizinische Zentral-Zeitung 1912, No. 24.

\* ) Compare Merck's Report 1911.

**Veronal and Veronal-Sodium.**

Attention has been directed during the last few years to the marked sedative action of veronal in the treatment of sea-sickness. The good results which have been obtained by the employment of this drug make it more and more evident that veronal constitutes a specific against sea-sickness and the nearly allied train-sickness. This has been discussed during the past year by Frank, M. Gerson, I. W. Brewer, Coulomb, J. Godart and Schepelmann. Schepelmann, in a most noteworthy paper upon sea-sickness, has thrown much light upon the etiology, pathogenesis and treatment of this affection. According to him, veronal has proved superior to all other drugs, both as a prophylactic and as a curative. It is best prescribed in 0.5 gramm (7½ grains) tablets, which are to be well chewed and swallowed with a little water. Veronal-Sodium is less suitable, for, according to Schepelmann, its alkaline taste may give rise to vomiting, especially in the prodromal stage. On a rough sea-passage the author has given 0.5 gramm (7½ grains) of veronal as a prophylactic, with the result that in many cases sea-sickness did not occur; for the treatment of actual symptoms he gave 0.75 to 1 gramm (12–15 grains) with good results.

Frank confirms the statement that veronal-sodium may give rise to vomiting, however, he found that this effect was entirely absent when it was given in cachets. He prescribed 0.2 to 0.5 gramm (3–7½ grains) of veronal or veronal-sodium 3 times a day, and in almost every case obtained a good result. Retching ceased, the headache grew less and a desire was felt for a moderate amount of food. Gerson, in opposition to the two authors mentioned above, declares that his patients did not complain of the unpleasant taste of veronal-sodium. He administered the preparation in the form of 0.5 gramm (7½ grains) tablets and obtained very good results. If the sickness has reached the stage at which the stomach is no longer able to retain the drug, he believes that some good may be done by administering the

Frank, Klinisch-therapeutische Wochenschrift 1912, No. 38.

Gerson, Münchener medizinische Wochenschrift 1912, No. 14.

Brewer, Therapeutic Gazette 1912, 15<sup>th</sup> June.

Coulomb, la Clinique 1912, No. 10.

Godart, le Scalpel 1912, No. 25.

Schepelmann, Die Seekrankheit, Berlin 1912. (Published by Dr. W. Rothschild.)

drug in the form of suppositories. According to Coulomb, it may in cases of this kind be applied as a solution 1 in 150. Brewer and Godart also give veronal and veronal-sodium a special position in the treatment of sea-sickness.

The value of veronal as a hypnotic has been discussed by E. Bloch, Dornblüth and R. Hutchison. Bloch prescribed it for nervous insomnia with very satisfactory results, so long as there was no considerable degree of excitement by day. Dornblüth administers veronal in cases in which the first hours of sleep are fairly normal and the later hours disturbed, and veronal-sodium in cases in which difficulty is experienced in falling asleep. He emphasises the absence of toxic action with normal doses (0.5 gramm [7½ grains]) of veronal. Hutchison considers that 0.3 gramm (5 grains) of veronal usually suffice, as the drug acts fairly promptly.

For gynaecological operations, S. Stocker recommends combined anaesthesia, the so-called veronal-atropine-morphine-ether anaesthesia. It consists in giving the patient 0.5 gramm (7½ grains) of veronal on the evening before the operation in order to induce sleep. One hour before the operation the patient is given a subcutaneous injection of 0.0005 gramm (1/125 grain) of atropine and 0.01 to 0.02 gramm (1/6 to 1/3 grain) of morphine, according to her constitution. The morphine is intended by its soporific action to supplement the ether anaesthesia; the atropine is intended to diminish the secretion of saliva and to counteract the effect possessed by morphine of causing vomiting. This combined preparation for ether anaesthesia possesses the following advantages: the stage of excitement is almost completely eliminated, only 5 to 10 minutes elapse from the commencement of administration of ether until the stage of tolerance is reached, there is no secretion of saliva, no vomiting occurs during anaesthesia and in only 20 p. c. of the cases after anaesthesia, and pneumonia does not supervene. Even patients suffering from pulmonary diseases may safely be anaesthetised by this method and also elderly people, but not children under 10 years of age, as they are very sensitive to alkaloids.

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Bloch, Medico 1912, No. 47.

Dornblüth. Die Schlaflosigkeit und ihre Folgen. 1912. Published by Veit & Co., Leipzig.

Hutchison. The Clinical Journal 1912, 9<sup>th</sup> August.

Stocker, Gynæcologia Helvetica 1912, Vol. 12, p. 207.

J. Zeisler reports a case of veronal idiosyncrasy. After giving 3 doses of veronal to a patient aged 30, there was itching of the glans and foreskin and inflammation lasting for several days.

A combination of veronal-sodium with phenacetin and codeine, so-called veronacetin, is recommended by M. Baer as a hypnotic and sedative. It is put on the market in the form of tablets. Each tablet contains 0·15 gramm (2 $\frac{1}{3}$  grains) of sodium diethyl-barbiturate, 0·125 gramm (2 grains) of phenacetin and 0·0125 gramm ( $\frac{1}{5}$  grain) of codeine phosphate. One to two tablets are given for a dose.

Another combination, that of veronal with chloral hydrate, is said by K. Halbey to be extremely efficacious. The narcotic effect is best obtained by giving first 0·5 gramm (7 $\frac{1}{2}$  grains) of veronal, and half an hour later 2 grammes (30 grains) of chloral hydrate. In extreme restlessness the author gave as much as 0·8 to 1 gramm (12—15 grains) of veronal.

I feel it my duty to point out that inferior substitutes for veronal are put on the market, as Mundici has recently shown. The author examined various preparations purchased in the open market and found among them three grossly adulterated preparations. One consisted of 50 p. c. of veronal, 30 p. c. of sulphonal and 20 p. c. of a mixture of trional and pyramidon; another consisted of 64 p. c. of veronal and 36 p. c. of phenacetin, and a third of 12 p. c. of veronal, 43 p. c. of sulphonal and 45 p. c. of acetanilide. The author met with similar frauds among other special preparations. Coronedi obtained similar results in his examination of substitutes, among others those for diuretin. In place of a content of 40 p. c. of theobromine, he found only 11 to 32 p. c. in a number of preparations.

### Yeast.

H. Prager-Heinrich and K. Seegers report upon yeast preparations. According to Prager-Heinrich, Xeras e\*),

Zeisler, Journal of the American Medical Association 1912, 29<sup>th</sup> June.  
Baer, Münchener medizinische Wochenschrift 1912, No. 9.

Halbey, Psychiatrisch. neurologische Wochenschrift 1912, No. 13.

Mundici, Bollettino chimico farmaceutico 1912, Vol. 51, p. 707.

Coronedi, Il Morgagni 1912, No. 5 and 6.

Prager-Heinrich, Therapie der Gegenwart 1912, No. 12, p. 537.

Seegers, Therapie der Gegenwart 1912, No. 12, p. 539.

\* Compare Merck's Reports 1910 and 1911.

which represents a mixture of yeast and kaolin, is a highly efficacious drug in all varieties of leucorrhœa; it only failed in 7 p.c. of all cases. The authoress used it in about 100 cases of leucorrhœa, in which the discharge was due to gonorrhœa, other inflammatory processes, or misplacements of the uterus, chlorosis or tuberculosis. In the majority of cases there was a history of previous gonorrhœa; and in a few cases there was no demonstrable cause. The powder was applied by means of a speculum, through which the cervix and the vaginal wall were first cleansed, the xerase being then poured in and distributed in a suitable manner. An insufflator is said to be unpractical, because it does not readily allow the introduction of the necessary large amount of powder. After 24 hours one or two irrigations with chamomile infusion were made. Xerase was applied on alternate days. Even in chronic gonorrhœal leucorrhœa, this troublesome condition was terminated in 10 to 20 sittings. This method of treatment never gave rise to disease of the adnexa, nor did the authoress observe a recurrence among a series of her patients in the course of a year. A few cases of chronic endometritis were also successfully treated by means of xerase.

Among other well known preparations of yeast, Seegers tested a new dry preparation of yeast, known as "Biozyme". It has proved to be equivalent in fermentative power to fresh yeast. The author did not carry out therapeutic experiments with the preparation.

### **Yohimbine.**

Lissmann advocates the use of yohimbine in the treatment of impotence, giving theoretical and practical reasons for his suggestion. In his opinion excitants for the cohabitation centres must exist, similar to those acting upon the heart, skin, bowel, etc. He cites yohimbine as suitable for the purpose, for numerous experiments in veterinary medicine have shown that it gives rise to a flow of blood to the external genitals, causes the blood pressure to fall, increases the tactile sensibility of the genitals and produces vasodilatation of the renal and cutaneous vessels. In man, as in animals, cases of impotence may be favourably influenced by yohimbine so

long as the impotence is due solely to exhaustion of the cohabitation centres. The unsatisfactory results frequently obtained by internal or subcutaneous administration may be due to the method of administration or application. As Cathelin had obtained good results in impotence by the epidural injection of simple saline solution, Lissmann tried the same method of application of yohimbine. The author's first trial justified his assumption that yohimbine must intensify the action of epidural injections of saline solution. The case was that of a man aged 35, whose power of erection was exhausted and who had undergone all kinds of hypnotic, physical and dietetic cures without success. The first epidural injection of 30 c. c. of saline solution and 10 drops of 2 p. c. yohimbine solution resulted in distinct improvement on the following day, and the continuation of the medication at definite intervals led to satisfactory erectile power. The author obtained an equally favourable result in the majority of cases subsequently treated in a similar manner. The author specially emphasises the fact that in the seven cases successfully treated by him the centre for erection was alone at fault, the patients never having suffered from precipitate ejaculations. In forms of impotence accompanied by *ejaculatio præcox* and in nocturnal emissions, on the other hand, the epidural injection of yohimbine did harm.

G. Fritsch, in view of further favourable results of the treatment of urogenital disturbances of elderly people by yohimbine, again\*) draws the attention of medical practitioners to the use of yohimbine as a nerve tonic. Its beneficial effect in these cases is also shown in a communication by W. Karo. The author did not, however, prescribe it internally like Fritsch, but by intragluteal injection. His patients (8 cases) all showed the clinical picture of enlarged prostate; there was polyuria, frequent, painful micturition and the residual urine was absent or inconsiderable in amount. The size of the prostate varied. The age of the patients varied between 54 and 67 years. The specific action of yohimbine on the disturbances of micturition was manifest, for all the patients, who had not been informed of the object

Fritsch, Deutsche medizinische Wochenschrift 1912, No. 42, p. 1980.

\*) Compare Merck's Report 1911, p. 455.

Karo, Zeitschrift für ärztliche Fortbildung 1912, No. 4, p. 112.

of the treatment, stated that the intervals between micturition were prolonged. In 6 out of 8 cases nocturnal micturition ceased entirely. At first the author gave a daily injection, but from the second week onwards he gave an injection on alternate days. The course of treatment took, on an average, 7 weeks. Untoward secondary effects of yohimbine were not observed in a single case.

Hübner recommends that the prolonged use of yohimbine should be accompanied by repeated examination of the urine. In experiments on rabbits, he found that the continuous administration of yohimbine caused the excretion of a slight amount of albumin, or gave rise to slight anatomical changes.

### Zebromal.

After Ellinger and Kotake had shown by pharmaceutical experiments that zebromal\*) is superior to other modern preparations of bromine, inasmuch as it allows sufficient amounts of bromine to be introduced into the organism, produces practically as great accumulation of bromine or displacement of chlorine, more especially in the blood, as sodium bromide and does not give rise to secondary effects on the nerves of taste, the digestive tract and the heart, P. Jödicke has carefully investigated the therapeutic effects of the drug. He gave the new preparation chiefly to epileptics who had for months or years taken sodium bromide with varying results. He was thus enabled to compare the action of zebromal with that of the alkaline bromides in the same patients. By administering 4 to 5 tablets a day\*\*) he obtained satisfactory results in every case. In some patients the convulsive attacks occurred less frequently than when sodium bromide was used. No injurious effect on cardiac activity or on the digestive organs was observed; the diminution of fits was usually accompanied by an increase in weight and an improvement in the general health. In one case of very severe epilepsy the author was unable to obtain the desired

Hübner, Dermatologische Zeitschrift 1912, Vol. 19, p. 863.

Ellinger-Kotake, Archiv für experimentelle Pathologie 1911, Vol. 65, p. 87.

\*) Compare Merck's Report 1911, p. 210.

Jödicke, Münchener medizinische Wochenschrift 1912, No. 7, p. 354.

\*\*) 1 tablet corresponds to 1 gramme of zebromal or 0.48 grammes of bromine.

result by the administration of zebromal, but in similar cases he succeeded in bringing about intervals of several days between the fits by the administration of 8 tablets a day.

Bromine acne was never observed. On the contrary, this symptom of bromism frequently disappeared under treatment by zebromal in patients who had previously taken alkaline bromides. Zebromal appears to be specially indicated in those cases in which the appearance of toxic symptoms necessitates the discontinuation of alkaline bromides, but in which the complete omission of bromine preparations is inadvisable. Jödicke reports that the successive administration of 6 to 1 tablets a day completely cured the troublesome cutaneous affections in a number of patients upon whom the experiment was carried out. The skin regained its normal gloss and the dulled mentality was replaced by greater psychic animation. The beneficial result was even more manifest when sodium chloride was simultaneously applied, both externally and internally.

In the author's experience, to reduce the number of fits in the mildest cases of epilepsy, in which months or years elapse between the attacks, 1 to 2 tablets a day may be recommended; for fairly mild cases, in which the fits occur about once a week, 3 to 4 tablets may be given; but in the bulk of epileptics, in which several fits occur weekly, no benefit can be expected from less than 4 to 7 tablets a day.

### Zinc Chloride.

In the experience of P. Mocquot and J. Mock, suitable treatment by means of zinc chloride is more successful in many cases of chronic metritis than is the customary treatment by curettage. They therefore recommend, in place of the latter, injections of 1 to 3 c.c. of a 30 p. c. solution of zinc chloride into the uterus, or of a 40 p. c. solution in haemorrhagic metritis. As these injections are painful, the uterus should be previously rendered insensitive by injections of cocaine solution. The injections should be administered by means of a Braun's syringe. After the application, the patient should remain resting for 12 to 24 hours. The injections are repeated after a period of a few days to two

weeks, as required. This treatment is said to be preferable to curettage on account of its simplicity and its harmlessness. The authors' statistics show that zinc chloride injections produced far better results than are usually obtained by curettage.

### Zinc-Perhydrol.

Zinc-perhydrol\*), which in a brief space of time has gained for itself general notice and recognition in the treatment of wounds and ulcers, was further investigated in the past year by E. Brodfeld and R. Müller. Müller reports a case of perforating ulcer which was healed by treatment with zinc-perhydrol. The author caused the ulcer, which was 3 cm. deep and which, as a consequence of purulent disintegration of the tissues, extended to the periosteum of the calcaneum, to be washed out daily with perhydrol (1 p. c.  $H_2O_2$ ) and sprinkled with zinc-perhydrol by means of an insufflator. A dressing of bismuth subgallate and vaseline (1:10) was then applied, but this, according to the author, did not affect the result. The first result was manifested by a rapid deodorising effect, with shedding of necrotic fragments and diminution of secretion, the wound becoming smaller. There was only slight granulation formation. Healing occurred after about two months, leaving a depressed scar.

In Brodfeld's experience, zinc-perhydrol is equivalent in value to iodoform and superior to its substitutes in the treatment of ulcers of the leg and of venereal ulcers; it is also preferable to iodoform on account of its freedom from odour. This is of special advantage in ambulatory practice. But, before treatment by zinc-perhydrol, virulent, copiously suppurating ulcers must be transformed into avirulent, clean wounds by cauterising with carbolic acid; they will then heal in a comparatively short time under the influence of zinc-perhydrol. No irritation of the surrounding area is produced, nor does dermatitis occur. The author also gained the impression that soft ulcers treated with zinc-perhydrol were less frequently complicated by buboes than were those treated by other substitutes for iodoform.

Brodfeld, Klinisch - therapeutische Wochenschrift 1912, No. 36,  
p. 1040.

Müller, Deutsche medizinische Wochenschrift 1912, No. 49, p. 2312.

\*) Compare Merck's Reports 1904—1911.

In incised buboes with copious purulent secretion, zinc-perhydrol not only diminished the suppuration in a short time, but it also promoted granulation formation, even in those cases which made no progress towards recovery when iodoform was used. The zinc-perhydrol was sprinkled over the wounds every second day, and these were well plugged with gauze.

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### The Assay and Standardisation of Digitalis Preparations

by

Professor Dr. R. Heinz

Director of the Pharmacological Institute of the University of Erlangen.

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E. MERCK, CHEMICAL WORKS, DARMSTADT, 1913.

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## The Assay and Standardisation of Digitalis Preparations.

By Professor Dr. R. Heinz

Director of the Pharmacological Institute of the University of Erlangen.

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The Pharmacological Institute of the University of Erlangen received a request from the Chemical Works of E. Merck in Darmstadt to investigate physiologically the efficacy of the digitalis preparations manufactured and put on the market by that firm, as it were "to standardise them physiologically". I consented the more readily to this request as I have recently devoted myself to the physiological standardisation of drugs the chemical composition of which is not known, or only partially determined. It is generally recognised that the physiological standardisation of the various digitalis preparations ("in the widest sense", including the strophanthus preparations and the — more or less pure — individual substances, such as digitalin, digitoxin, digalen, strophanthin, etc.) is required. The practitioner who prescribes digitalis preparations for his patients has undoubtedly the right to demand exact information as to the efficacy of the drugs supplied to him by manufacturing chemists.

In the following article the process will be explained by which digitalis preparations are tested in the Pharmacological Institute at Erlangen. The process is carried out in connection with the methods already known; this is manifestly necessary, in order that the results may be compared with those obtained by other methods; but the tests are extended in

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\* ) Besides the chemical and galenical preparations of digitalis hitherto indicated in my lists, I shall, in compliance with a widely expressed wish, add preparations the normal efficacy of which has been established by physiological tests. These tests will be carried out by the Director of the Pharmacological Institute of the University of Erlangen, Professor Dr. R. Heinz, according to the methods described in this article. The result of the tests will be noted on the bottles, which will be sealed, and the contents guaranteed.

E. Merck.

many directions, so that the determination of the "standard" takes into account not only quantitative differences in the degree of efficacy, but also qualitative differences in the manner of action, which may vary considerably among the various forms of digitalis preparations.

### I. Theory of the Method of Standardisation.

A useful method of assay of digitalis preparations should be clear and simple; clear, so that everyone may understand the meaning of the test, simple, so that it may be easy to control the results obtained. All methods at present in use take as a criterion of the strength of action the cessation in systole of the ventricular beat of the frog's heart. The substances acting like digitalis possess the peculiarity of causing stoppage of the frog's heart by a maximum, and to a certain extent convulsive, contraction of the cardiac chamber. The degree of efficacy of the digitalis preparation under consideration is determined from the amount of the dose required to call forth this action\*).

The earliest method generally employed in Germany to determine the value of digitalis leaves of different origin was that of Focke. To carry out his method a 10 p. c. infusion is prepared from broken up digitalis leaves. A fixed amount of this is injected subcutaneously into land frogs (*Rana temporaria*), weighing about 30 grammes. The frog is bound to a small board and the heart laid bare for inspection. The amount injected should be about  $\frac{1}{40}$  of the body-weight of the frog (e. g., a frog weighing 30 grammes would receive 0.75 c. c. of the 10 p. c. infusion). The heart is watched and the time noted at which the ventricle stops beating in systole. In normal frogs this occurs on an average in 10 minutes, when digitalis leaves of medium strength are used. If

the weight of the frog =  $p$  (in our case 30 grammes),  
the amount injected =  $d$  (in our case 0.75 c. c. of the  
10 p. c. infusion),  
the time which elapses until the ventricle stops beating  
=  $t$  (= 10 minutes),

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\* ) For a criticism of the method compare Part II.

and if  $p$  be divided by  $d$  times  $t$ , then, according to Focke's calculation, the result will be:

$$\frac{p}{d \cdot t} = (\text{"Valor"} = \text{Value of the preparation})$$

$$\text{in our case } V = \frac{30}{0.75 \cdot 10} = 4.$$

Even in less favourable years digitalis leaves have, on an average, the valor 4, and Focke therefore takes valor 4 as the "normal value". Thus, digitalis leaves of valor 6 are very strong, those of valor 2 very weak specimens; by mixing together equal parts of the two, a preparation of valor 4, i. e., of normal value, may be obtained.

The execution of the method is not so simple as might be inferred from the above description. Certain precautions must be observed in order to arrive at accurate results. The chief difficulty lies in the fact that the experimental animals behave very differently at different times and under different conditions (nutrition, temperature, etc.). Above all, quite different doses are required in summer and in winter in order to produce the same action. Focke attempts to meet this difficulty by keeping the frogs warm in winter (in a "hot box"), regulating the temperature so that the animals have a pulse rate of about 60 per minute. But even this does not guarantee uniform behaviour; Focke himself declares that only those animals should be used for the test which in a previous experiment with a known preparation show the expected action.

But Focke's method has a further fault, which renders it unsuitable for general use. In deriving the valor  $V$  from the equation

$$V = \frac{p}{d \cdot t}$$

the time  $t$  plays far too important a part and may lead to grave errors. Focke's method is, so to speak, a "very acute" method. The stoppage of the ventricle in systole should occur, on an average, after only 10 minutes! If for any reason absorption is delayed, so that — the action being in other respects equal — definite stoppage of the ventricle is only observed after 15 minutes, the valor seems to be reduced out of all proportion:

In 10 minutes:

$$V = \frac{30}{0.75 \cdot 10} = 4.$$

In 15 minutes:

$$V = \frac{30}{0.75 \cdot 15} = 2.66.$$

Now variations in absorption may very readily occur and do, in point of fact, frequently occur. Under these circumstances, an interval of 10 minutes until the final effect is far too short, especially if large quantities of fluid have been injected. If 1 c.c. of water is injected into a lymph-sac of a frog (for example into a lymph-sac of the thigh), it will be found full to overflowing after 5 minutes and will contain plenty of water even after 10 minutes. Thus it makes a great difference in the commencement of action (even though it may not affect the final action) if 0.01 milligramme of strophanthin, for example, is injected dissolved in 0.1 c.c. or in 1 c.c. of water; in the former case the action commences much sooner than in the latter. This shows that in comparative examinations the substance to be tested should be injected in as little water as possible (not more than 0.5 c.c., but, on account of dosage, not less than 0.1 c.c.).

Substances, however, exist among the digitalis bodies, which — apart from the concentrations of their solutions — are in themselves absorbed more slowly than others. With these no action whatever can be expected within 10 minutes. Thus, though Focke's method may be suitable for comparing similar preparations (for example digitalis infusions of different origin), it is quite unsuitable as a general method for the assay of digitalis bodies.

While Focke places in the foreground the time required to cause stoppage of the ventricle in systole, Gottlieb determines the smallest dose which will cause cessation in systole of the heart of a temporaria weighing 30 grammes within half to three quarters of an hour. Gottlieb also first determines the degree of efficacy of "natural" digitalis preparations, of infusions, extracts, etc., of digitalis leaves (of different origin or prepared in a different manner). He prepares solutions containing definite amounts of the original substance and injects decreasing quantities, corresponding, for example, to  $\frac{1}{10}$ ,  $\frac{1}{20}$ ,  $\frac{1}{30}$ — $\frac{1}{80}$ ,  $\frac{1}{90}$ ,  $\frac{1}{100}$  gramme of the solid substance. He observes which amount causes stoppage of the frog's ventricle in systole half to three quarters of an hour after injection. Gottlieb names this

dose the "unit of action". One grammie of digitalis leaves of medium strength, used in the form of infusion, contains, according to Gottlieb, 40 to 50 units. The valency of digitalis leaves of this kind is therefore 40—50. But species of digitalis leaves exist, which (in the form of freshly prepared infusions) possess a valency of 100, or more.

Gottlieb, it will be observed, allows much greater scope for the commencement of the "final effect" than does Focke, i. e., half to three quarters of an hour. C u s h n y has extended this time to one hour. These are all — even though not "very acute" — yet "acute" methods of digitalis standardisation. All the stages of action of digitalis, the "therapeutic" as well as the "toxic" stage are expected to run their course within half to one hour! But in man the therapeutic effect of even large doses of digitalis only takes place after many hours, up to 24 hours. This is certainly not merely due to slow absorption; it is more probable that certain digitalis bodies require a longer time, even after they have been absorbed, before their effect on the cardiac muscle becomes manifest. These slowly acting bodies (for example digitalin)\*), when given in certain doses, appear to have no effect during the first hour, whereas — after 3, 6 and more hours — they undeniably cause stoppage of the ventricle in systole and thus lead to inhibition of the circulation and to death. Therefore, in order that all digitalis bodies may be assayed according to a uniform method, it is essential that the interval which elapses up to the stoppage of the ventricle should be extended still further.

Houghton has taken this fact into consideration. His method, which is largely used in America, consists in injecting into frogs decreasing amounts of the substance to be examined and noting the smallest dose which is just fatal to a frog weighing 30 grammes within 12 hours. This method is undoubtedly very simple. At first sight it might appear too summary and unscientific. We do not wish to ascertain the fatal dose of the drug, but to investigate the specific action of the drug on the heart. But the cessation of the circulation caused by the stoppage of the ventricle leads to death and it is only necessary to make sure that the action on the heart is not accompanied by a toxic effect endangering life. This assurance is indispensable, but it is estab-

\*) Compare below.

lished as far as the known digitalis substances are concerned. Houghton's method is positively the only general method which allows a comparison to be drawn between the intensity of action of all digitalis bodies, the rapidly acting and the slowly acting ones.

In America still more important innovations have been introduced for determining the value of different digitalis bodies. Special attention has been drawn above to the fact that frogs show varying behaviour under different conditions and at different times. Immediately after copulation the animals are very weak and are little able to resist poisons. Before laying the eggs, the ovaries of the females become greatly swollen, so that the body-weight is considerably increased — solely by the absorption of water. Both kinds of animals are useless for our experiments. From June to October frogs of the same weight and of the same species behave in approximately the same manner. But during the winter months the behaviour of the animals is quite different from that in the summer. They are well suited for physiological experiments, but their sensibility is quite different from that shown in the summer — in some respects it is less, in others greater — and to arrive at the same effect totally different doses must be given. It is not sufficient, as suggested by Focke, to transfer the animals to a warm place for some time before carrying out the experiment in order that their pulse rate may reach 60—64 per minute (as in summer). There still remain great, and in isolated cases, variable differences. Therefore in every single case the sensitiveness of the frogs selected for the experiment must be tested. This must be carried out by the use of a digitalis substance having an accurately known, typical action; and the substance chosen must be uniform, chemically pure, readily prepared and of definite character and must keep without alteration. Gratus-Strophanthin (identical with crystalline ouabaïn) has been suggested as a body for comparison, and has been fairly generally accepted. g-Strophanthin\*) meets the demands mentioned above. It may at any time be readily prepared in a pure form (as a crystalline body having a definite melting point and other constant characteristics) from the seeds of Strophanthus gratus, which

\*) Compare Merck's Report 1911, p. 123.

are plentiful; and it does not alter even after having been kept for years.

In every series of experiments (whether in winter or in summer) frogs as similar and as equal in weight as possible are injected with decreasing doses of g-strophanthin on the one hand, and of the body under investigation on the other hand. The smallest dose of the two bodies which causes death within 12 hours is thus found. Note should also be taken of those doses of the two bodies which cause cessation of the heart in systole in exactly one hour (and also whether, and as the result of what dose, the heart stops beating within 10 minutes, for comparison with the one hour method and also with Focke's method). Thus two (or three) comparative values are obtained. Thus, for example (summer experiment)

	g-strophanthin	digitalatinum verum
the smallest fatal dose:	0.025 milligramme (in 2 hours)	0.25 milligramme (in 12 hours)
in 10 minutes   Dose effecting   0.05 milligramme   1.5 milligramme		
in 1 hour   stoppage of   0.1 milligramme   not effected even   heart:                                          by 15 milligrammes!		

This shows: that g-strophanthin is capable of acting very rapidly. The dose effecting stoppage of the ventricle in systole in 10 minutes is 4 times the minimum fatal dose; that effecting stoppage in one hour is double the minimum fatal dose. The minimum fatal dose is 0.025 milligramme and causes death in two hours. The digitalatinum verum under examination is markedly slow in action: it is incapable of effecting systolic stoppage of the heart in 10 minutes — even by giving 600 times the fatal dose. In order to cause systolic stoppage in one hour 6 times the fatal dose is required (as compared with twice the fatal dose of g-strophanthin). The smallest fatal dose (which brings about the "final effect" only after 12 hours) is 0.25 milligramme, i. e., 10 times greater than g-strophanthin.

For "standardisation" we used the relationship between the smallest fatal doses of g-strophanthin and of digitalin, viz., 10:1; not the absolute values, as these differ widely at different times (in winter, for example, as compared with summer), whereas the relationship to one another of the

doses of the two bodies remains approximately the same. Instead of the figures 10:1 we may of course just as well give 100:10 or 1000:100, according to choice. It has been agreed in America to give to g-strophanthin the figure 1000. Accordingly the digitalinum verum under examination would receive the value 100.

In the Pharmacological Institute of the University of Erlangen the digitalis bodies are examined in the manner described above and are compared with g-strophanthin, which is adopted as the standard. The value "One" might be allocated to g-strophanthin, but in that case the comparative figures would fall too low. For even with the standard value "one thousand" relatively small figures are obtained for the digitalis samples and for the galenical preparations of digitalis, provided the method is carried out in a uniform manner and the absolute amount by weight of the drug or of the galenical preparations (dry extract, fluid extract, tincture, etc.) is taken to represent the dose, and not the amount of active substance (of digitoxin, for example) or of solid substance (for example fluid extract 1:1, or tincture of digitalis 1:10, etc.) contained. Digitalis leaves (of different origin and of different age) are examined in the form of infusion. The infusion must, of course, always be prepared in exactly the same way. The (dried) digitalis leaves are finely powdered. 1 gramm of the (sifted) powder is weighed and placed in a small glass flask; 19 c. c. of boiling water are added and the flask is placed for 5 minutes on a water-bath, and the contents stirred frequently. The contents of the little flask are poured into a measuring glass of 20 c. c. capacity, the flask is rinsed with a few drops of water and the total volume is made up to 20 c. c. Thus 1 c. c. of the infusion contains the soluble constituents of exactly 0.05 gramm of digitalis leaves. Then 0.5—0.4—0.3—0.2—0.1 c. c. of this 5 p. c. infusion are injected. Let us assume that 0.2 c. c. is the smallest fatal dose and 0.5 c. c. the smallest dose which effects stoppage of the ventricle in systole in one hour. Assuming that the simultaneous estimation of g-strophanthin on similar frogs (of equal weight) gives as results 0.005 milligramme and 0.01 milligramme (experiments carried out in winter). 0.2 c. c. of the 5 p. c. infusion corresponds to 0.01 gramm of digitalis leaves, 0.5 c. c. corresponds to 0.025 gramm. Thus the ratio is as follows:

the smallest doses acting in 1 hour = 25,000:10, the smallest fatal doses = 10,000:5, viz., the efficacy = 1:2000. If g-strophanthin is given the value 1000, as agreed upon, then the value of the above preparation of digitalis will be 0.50.

Let us assume that a tincture of strophanthus from a certain source is to be examined. 1 c. c. of the tincture is made up to 10 c. c. by adding 9 c. c. of water. Then 1 c. c. of the mixture will contain 10 p. c. of the original tincture (We do not refer to the amount of solid substance contained, as this is unknown to us, though as a rule tincture of strophanthus is prepared in the proportion 1:10.) Supposing 0.4 c. c. of our solution effects cessation of the heart in systole in one hour, and 0.2 c. c. is the minimum fatal dose. This corresponds to 0.04 and 0.02 grammes of the original tincture. The simultaneous examination of g-strophanthin yields as corresponding doses 0.01 and 0.005 milligramme. The relationship between the minimum fatal doses is therefore 5:20,000 or 1:4000. Thus the value of the tincture of strophanthus is 0.25. Should the tincture of strophanthus have been actually prepared in the proportion of 1 gramme of seeds to 10 grammes of tincture, it may be said that the strophanthus seeds under consideration possess the value 2.5.

The method described, as has been noted, gives comparative figures. This may appear unsatisfactory to some. A comparative figure affords no direct representation of the method of action of the preparation. We require concrete figures, statements of absolute amounts. If we designate the smallest efficacious dose (i. e., fatal to the frog) "unit of action", and this dose (compare above "summer" experiment) is 0.025 milligramme for g-strophanthin and 0.25 milligramme for digitalinum verum, then 1 gramme of g-strophanthin would contain 40,000 "units of action", and 1 gramme of digitalinum verum 4000 units. This method of expressing the value may appear more satisfactory to many. But the efficacious dose of g-strophanthin (and of digitalin, etc.) varies in summer and winter: in the summer frog 0.025 milligramme, in the winter frog 0.005 milligramme. According to this, 1 gramme of g-strophanthin would contain 40,000 units in summer, and 200,000 units in winter. Which of these is to be considered the standard term? This should be settled by international agreement. If it should appear — from experiments carried out according to a definite plan in the laboratories of dif-

ferent countries — that during the months of June to September the minimum fatal amount of g-strophanthin is approximately the same for the normal, freshly captured land frog (*Rana temporaria*) and that this dose is, for example, 0.025 milligramme for frogs weighing 30 grammes, this dose could be regarded as the "international unit of action" for the normal frog; thus, 1 gramme of g-strophanthin would contain 40 000 international units. In all determinations of the value, therefore, the effective dose of g-strophanthin would first have to be established. Should this differ from the dose required by the normal frog, if, for example, it is found to be 5 times smaller, then all values in the series under consideration must be multiplied by the factor  $\frac{1}{5}$ . The actual valuations would then be carried out exactly as described above.

Thus it is seen that it is merely the manner of expression which differs in the method of assay. In every case reference must be made to a stable standard preparation, which can be obtained everywhere and is always the same (viz., gratus-strophanthin), and the preparation to be tested must be compared with it, or — as an alternative — the sensibility of the experimental animal must be thoroughly investigated. But it is certainly most desirable that an international standard should be established, whether by units of action on the normal frog or by taking as a basis the figure 1000 as the value of gratus-strophanthin. In the United States the latter procedure has been adopted, and we also (compare above) favour this designation.

In contradistinction to the "acute" methods, we make use of the protracted method (observation up to 12, or if necessary 24 hours), and this is also the method chiefly employed in America. In our experimental procedure, besides ascertaining the minimum dose which is fatal through stoppage of the heart, we also obtain the "acutely acting" dose, which leads to systolic cessation in one hour. This serves, when required, for comparison with other one hour methods. At the same time we make another observation, which is of great practical importance: We note which preparation acts rapidly and which shows protracted action. Strophanthin is a rapidly acting body: the first effects become evident very soon after the injection and the whole symptom complex, therapeutic plus toxic stages, runs a very rapid course. Digitalin, on the other hand, takes a long

time to develop its effect and the final stage only occurs after many hours. In treating sudden weakness of the heart we naturally resort to a rapidly acting drug (strophanthin); on the other hand, bodies having a very protracted action readily tend to exhibit a cumulative action.

## II. Criticism and Elaboration of the Method.

All the methods of determining the value of digitalis preparations which have been in use hitherto, as noted in the foregoing, make use of the cessation of the ventricle of the frog's heart in systole to characterise the action of the drug. The systolic cessation represents a spasmodic, lasting contraction of the ventricle, and is thus a toxic action. A heart which has ceased to beat is naturally unable to maintain the circulation and death ensues. In the action of digitalis we distinguish two entirely different stages: the therapeutic stage and the toxic stage. In the therapeutic stage we note retardation of the heart beat with greater diastolic dilatation of the cardiac cavity, so that the heart is enabled to draw more blood from the venous system; and secondly increased energy of the ventricular contractions, so that the increased contents of the ventricle can be thrown with greater force into the arterial system. The toxic stage shows irregularities of the heart beat and a diminished pulse volume. The ventricle is no longer capable of undergoing sufficient diastolic dilatation, it shows ever more tendency to continuous contractions, until finally it drives out no more blood and stops beating in the position of maximum contraction. The toxic stage — as regards circulation of the blood — forms the antithesis of the therapeutic stage. In man we anxiously seek to avoid the toxic stage. And yet from the cessation of the ventricle in systole, the crowning point, as it were, of the toxic effect, it is thought that an inference may be drawn as to therapeutic efficacy! And it is quite possible, indeed it is a matter of actual fact, that a relationship exists between the production of the characteristic muscular action on the frog's heart and the therapeutic effect upon the diseased cardiac muscle in man. But this relationship is not clearly manifest. Vegetable drugs, glucosides, etc., which in the frog give rise to typical systolic cessation of the heart, are not necessarily

suitable for the treatment of disease in man; and it is therefore manifestly insufficient to draw conclusions as to the "value" (in a general sense) of a digitalis preparation from the degree of action upon the frog's heart alone. The frog, in certain respects, shows quite different behaviour towards digitalis bodies from warm-blooded animals and man: In warm-blooded animals the ventricle never stops beating in systole; in the warm-blooded animal retardation of the pulse is not, as in the frog, brought about by action on the cardiac muscle, but by stimulation of the vagus centre (which slows the heart beat); in the toxic stage we observe — in place of increasing retardation of the pulse — greatly augmented pulse rate (by paralysis of the vagus endings in the heart).

Finally, in our experiments on frogs, we almost exclusively give subcutaneous injections. But in the human subject we administer digitalis preparations internally for the most part, very rarely subcutaneously, more frequently now by intravenous injection. In passing through the stomach some digitalis substances are more or less decomposed by the action of the digestive secretions, as for example the strophanthins, so that only a portion of the amount ingested can take effect. It is clear that the efficacy of the subcutaneous doses given to the frog cannot be compared with that of the doses given by mouth to man.

From these considerations it follows that in order to determine the true value of digitalis preparations experiments on warm-blooded animals must be taken into account. But a useful method of valuation must be simple, i. e., easily carried out and not too expensive as regards the use of experimental animals. In the Pharmacological Institute in Erlangen we use mice for experiments on a large scale on the assay of digitalis preparations. Acting on the assumption (which must be verified by preliminary experiments in the case of unknown, new bodies) that we are dealing with a digitalis preparation which acts as a pure cardiac poison, it is just as easy to determine the smallest dose acting fatally on account of stoppage of the heart, i. e., the "effective dose" in the mouse as in the frog. And there is the additional advantage that mice of the same breed, unlike frogs, do not behave differently in different seasons, but (with the same treatment and surroundings, good

feeding, suitable housing, avoidance of wetting, etc.) they behave in an identical manner.

In the first place, the smallest fatal doses of gratus-strophanthin, of the body under investigation and thirdly of digitoxin are determined in mice of equal weight. Digitoxin, like g-strophanthin, is an accurately defined, chemically uniform, crystalline, stable substance. It is perhaps more suitable as a standard preparation than g-strophanthin, at any rate for warm-blooded animals, or rather it would prove of value in the standardisation of a digitalis preparation, if its effect were compared with that of g-strophanthin as well as with that of digitoxin.

The wide differences in the course of action are far more evident after subcutaneous injection into mice than in experiments on frogs. Strophanthins: Gratus-strophanthin, Kombé-strophanthin and tincture of strophanthus show acute action, beginning and ending rapidly. The greatest contrast to this is afforded by digitalin, in which (even after several times the fatal dose) no effect is evident for many hours. The action of digitoxin is somewhat less protracted. But it is more similar to that of digitalin than to that of strophanthin; the action is by no means "acute"; it is extremely slow but not so markedly protracted.

When the smallest fatal dose given by subcutaneous injection has been ascertained, mice are given 1, 2, 4, 8 times the fatal dose by mouth. The procedure is as follows: The experimental animal (mouse) is transferred from its little single cage (simple little wire cage) to a clean glass — without food. After fasting for a few hours, it is given a food pill\*) which is impregnated with the selected dose dissolved in one drop of water. Being hungry, it eats the entire pill. Then, after one hour, for example, more food pills (e. g., 5 or 10) may be given, in order to find whether the digitalis preparation has a deleterious effect on the appetite (by causing injury to the stomach). Note is taken when or after which dose the earliest symptoms or (cardiac) death occur, and the time

\*) A fair number of these food pills are prepared, for example from pancake-dough, about  $2\frac{1}{2}$  mm. in diameter; they should be somewhat porous, so that they will readily absorb the fluid. A pipette is used which, when held vertically, delivers exactly 20 drops to 1 c. c. 1 drop of a 0.2 p. c. solution of digitoxin will, for example, contain  $\frac{1}{10}$  milligramme of digitoxin.

and dose are compared with the time and dose after subcutaneous injection. By means of this very simple procedure the following facts are established:

1. The intensity of action of subcutaneous injection, compared with that of g-strophanthin and digitoxin.
2. The mode of action, whether acute or delayed.
3. The relationship of action after administration by mouth and after subcutaneous injection.
4. The tolerance for the preparation when administered internally.

It is evident that the mouse method provides a much more exhaustive knowledge of the properties of the digitalis preparations than the frog method. It would be of great interest to carry out systematic comparative experiments on mice and frogs. Should it be found that the frog doses (smallest dose causing death by cessation of the heart in systole) and mouse doses (smallest fatal dose), when injected subcutaneously, run parallel to one another, as regards the principal preparations of digitalis and strophanthin, it might be possible to discard the frog method entirely and to use the mouse method in its place. This would have the enormous advantage that uniform experimental material would be ready to hand at all times.

The fact that strophanthin is partially decomposed in the digestive tract renders gratus-strophanthin unsuitable as a standard preparation for experiments on warm-blooded animals. It might be advisable to use digitoxin in its place. The best plan is to use both preparations for comparison. This may also be recommended because, as has been mentioned several times, there are two entirely different kinds of digitalis action, the one "acute", the other "protracted"; and because g-strophanthin and digitoxin are representatives of the two varieties of action.

In the frog method of determining the value of digitalis preparations it is taken for granted that the qualitative action of the different preparations is uniform. But this, as has been pointed out, is by no means the case. Neither the "frog method" nor yet the "mouse method" provides us with information regarding the therapeutic stage, i. e., as to the effect of small (non-fatal) doses, which alone are of importance in the treatment of patients. Elucidation of this point is most desirable, for even the well known digitalis substances

have not all been so minutely investigated that the details of difference in their methods of action are thoroughly understood. No reference is made here to the examination of the isolated hearts of cold-blooded or warm-blooded animals or to experiments in which fluids are caused to flow through blood vessels, etc. These experiments, though essential for the exhaustive analysis of the action of digitalis, are complicated in technique while much experience is required in order to criticise their results; this knowledge everybody cannot be assumed to possess. But it should be insisted upon that every digitalis preparation offered to the public, besides having been "standardised" according to the frog or the mouse method, should also be tested for its effect upon blood pressure. The blood pressure experiment is comparatively easy to carry out and is so clear that anyone at all conversant with animal experiments very soon learns to master it. Rabbits are the most convenient animals to use for blood pressure experiments. To bring about narcosis they are given urethane (1 gramm per kilo of body-weight). The blood pressure is measured in the carotid; the substance for investigation is injected into the jugular vein. A mercury manometer and a spring manometer are used to register the carotid pressure. The former indicates the variations in the blood pressure before and after injection, the latter furnishes the pulse curve, which gives important information with regard to the behaviour of the heart.

In investigating the circulatory effects the following questions are at issue: Does the preparation, besides acting upon the heart, also act upon the blood vessels, either directly on the wall of the vessel (causing the unstriped muscle to contract), or on the vascular nerve centre (stimulating it and thus causing general vascular contraction with consequent rise of blood pressure)? This is not the case with digitalis infusion, digitalinum verum, digitalein and digitoxin. With these we observe (in the therapeutic stage) only a slight rise of blood pressure, due to increased cardiac energy. Nor is it desirable that the blood pressure of a patient suffering from heart disease should be appreciably raised. Contraction of the vessels would increase the cardiac resistance and cause a greater amount of work to be demanded from the heart. But in chronic cardiac weakness (for which digitalis is prin-

cipally required) the debilitated heart is permanently near the limit of its capacity for work: a sudden great rise of blood pressure would overtax the heart and might suddenly paralyse it. Digitalis is such an excellent curative drug because it strengthens the heart without exacting too much work from it.

Strophanthin (Gratus and Kombé strophanthin), given to the rabbit in comparatively small doses, causes a great rise of blood pressure, or rather marked variations in pressure: a forcible high rise, then a rapid fall, then again rise and fall in irregular rhythm, and so on. The cause is not stimulation of the unstriped musculature of the vessels (which would lead to permanent high blood pressure), but peculiar forcible stimulation of the central vasomotor apparatus (true "delirium" of the vasomotor centres). These variations occurred after intravenous injection of 0.025 milligramme of g-strophanthin, while 0.01 milligramme was found to be the smallest effective dose. The consequences of injecting strophanthin are rapidly manifest, almost immediately after the injection; the variations in the blood pressure soon pass on (toxic stage) to lowered pressure with an irregular, quickened pulse (paralysis of the vagus) and in a few minutes death ensues. G-strophanthin is here also a rapidly acting drug. Thus strophanthin alone among digitalis preparations is suitable for effecting rapid relief in cases of dangerous cardiac debility and it is at present almost exclusively used for this purpose (in the form of intravenous injections). Our experiments show that effective and toxic (or fatal) doses lie comparatively close together, and the dosage must therefore be very carefully regulated.

In contradistinction to strophanthin, digitalis shows no acute action. Immediately after the injection, indeed even during the next hour, absolutely no changes occur either in the mercury pressure or in the pulse curve. The delayed action of digitalis, as already observed in the frog and the mouse, is thus not merely the consequence of slow absorption, but there actually exists a latency of action, i. e., although digitalin is circulating in the blood and can thus act directly on the heart, a fair amount of time is required before the digitalin molecule can unite with the molecule of the cardiac muscle, or before they can mutually act upon one

another; until, as a result of their interaction, an external effect, i. e., an alteration of function, becomes manifest. These experiments show clearly that digitalin is quite unsuitable for the treatment of acute cardiac weakness; and that the apparent absence of effect following a dose should not lead to a repetition or an increase of the dose in the course of several hours; for either then or after an indefinite period sudden death from heart failure may occur.

It is seen that blood pressure experiments on the rabbit give an insight into the various properties of, or differences between, the digitalis substances; and this is of the utmost importance for their valuation; i. e., for their rational employment at the sick-bed.

Experiments on cats are even more desirable than experiments on rabbits, provided that sufficient cats can be obtained for the experiments. Cats are far more sensitive to digitalis preparations than rabbits. The same applies to dogs, which are, however, in general too expensive to be used as experimental animals for the assay of digitalis substances. Cats react to much smaller doses of digitalis and at the same time show more striking circulatory changes. Certain secondary effects can also be better observed in these animals. For instance, intravenous injections of digitoxin give rise to violent retching movements in cats (strophanthin does not). This affords proof that the gastric symptoms, which occur after ingestion of digitoxin, are not only due to local causes (by irritation of the stomach), but are to some extent produced in the circulatory system. Cats are also very well suited for the detection of local injurious effects, especially in the gastro-intestinal canal. Gastric irritants readily produce vomiting in cats, while rabbits are unable to vomit. Digitalis leaves of different origin produce varying degrees of vomiting in cats. By a special method of extraction, the irritating substances (saponin-like in nature) can be withdrawn from the leaves. This purified preparation, "digipuratum Gottlieb", does not affect the stomachs of cats so as to cause vomiting. In the same way other digitalis substances may be tested and the presence or absence of an injurious effect upon the stomach noted; in this way knowledge is gained as to the "tolerance" of the preparation in question, which is of great clinical importance.

**Summary:** Procedure with regard to the assay and standardisation of digitalis preparations in the Pharmacological Institute of the University of Erlangen.

1. Decreasing amounts of the preparation to be tested and of gratus-strophanthin are simultaneously given by subcutaneous injection to a fairly extensive series of land frogs (*Rana temporaria*) of equal weight (if possible 30 grammes) and under the same conditions. The smallest dose of each substance is noted, which just causes death by stoppage of the heart. At the same time — for the sake of comparison with other "one-hour-methods" — the smallest doses are noted which produce stoppage of the ventricle in systole in the course of one hour. The smallest effective doses of the two bodies are compared with one another. The degree of effect is, of course, in inverse proportion to the size of the dose. Gratus-strophanthin is given the value 1000. For example, the smallest fatal dose is found to be

	g-Stro- phanthin	Digitoxin	Digi- talium ver.	Powdered Digitalis leaves
the ratio of the doses is	0.005 milli- gramme	0.025 milli- gramme	0.05 milli- gramme	0.01 gramme
the degree of effect is	$\frac{1}{5}$	$\frac{1}{25}$	$\frac{1}{50}$	$\frac{1}{10\,000}$
	or 1000	200	100	0.5

If the medicinal dose of any one of the four substances is known, then the doses of the other substances can be calculated. If in a certain case, for example, I should prescribe 0.3 milligramme of digitoxin as a single dose, then I should prescribe as corresponding doses

$$\text{of g-strophanthin } \frac{5}{25} \cdot 0.3 = 0.06 \text{ milligramme,}$$

$$\text{of digitalin. ver. } \frac{50}{25} \cdot 0.3 = 0.6 \text{ milligramme,}$$

$$\text{of digitalis leaves } \frac{10\,000}{25} \cdot 0.3 = 120 \text{ milligrams  
(0.12 gramme)}$$

2. Then in mice of the same breed — in the same way as in frogs — the smallest dose of g-strophanthin and of the substance under investigation are determined, the subcuta-

neous injection of which just causes death by stoppage of the heart. Then the dose is found which produces the same effect when administered by mouth. The doses "by mouth" and "subcutaneous" of each separate substance are compared with one another. Should it be found that in administration by mouth twice, 4 times, 8 times, etc., larger doses are required than by subcutaneous injection, this signifies that  $\frac{1}{2}$ ,  $\frac{3}{4}$ ,  $\frac{7}{8}$ , etc., of the amount of substance ingested has been destroyed by the digestive juices or has been prevented in some other way from being absorbed from the gastro-intestinal tract (for example, strophanthin compared with digitoxin).

3. In the mouse and in the frog note is taken of the interval of time up to the commencement of the earliest symptoms and up to the "end action", and it is thus found whether the method of action is "acute" (strophanthin) or "slow" (digitoxin), or "protracted" (digitalin).

4. Blood pressure experiments are carried out on rabbits with the preparation under investigation; g-strophanthin (having an acute action) and digitoxin (acting gradually) serving as preparations for comparison. In these experiments special attention is directed — apart from the general course of action and the relationship between "therapeutic" and "toxic" doses — to the behaviour of the vessels (whether or not contraction of the vessels with rise of blood pressure is present) and to that of the heart and the cardiac nerves (frequency and force of the heart beats, pulse curve, excitability of the vagus, etc.)

5. Blood pressure experiments by means of intravenous injections are carried out on cats, as the circulatory effects of the digitalis preparations and any secondary effects can be better observed in these animals than in rabbits.

Finally, the substance under investigation is given to cats by mouth, and from the occurrence or absence of vomiting, conclusions are drawn as to the tolerance of the drug or to its injurious effect upon the gastro-intestinal tract.

BUCHDRUCKEREI EDUARD ROETHER, DARMSTADT.

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